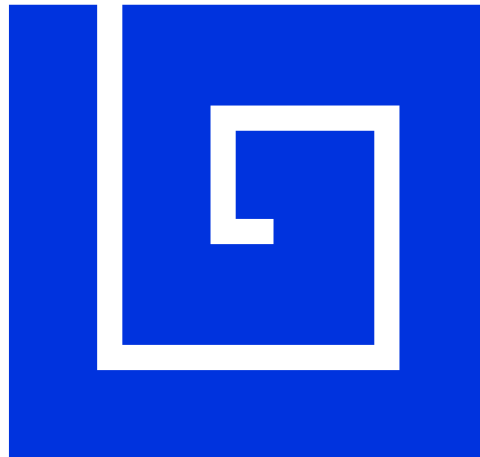


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EDITORIAL

TUULA KIESEPPÄ

Violence has touched us in various ways during the last two years. Russia's war of aggression against Ukraine shocked the world in February 2022. Since the war's onset, it has caused constant suffering and anger. The terror and hardship in Ukraine, the distress of refugees arriving all over Europe, including Finland, and the expanding menace of Russia have all overshadowed our lives. Although all of this has received special attention, we must not forget the other wars and crises going on in the world; bringing misery and exile, and the need for a cure.

Violence, as such, does not threaten us solely from the outside. We all are at least to some extent capable of violent acts. During the last year, there has been increasing news about violence involving street gangs and organized criminals in Finland. Furthermore, we have encountered unbelievable violence and humiliation among youths, and several most sad and devastating acts of domestic abuse. Overall, experiencing violence is still common in Finland (Statistics Finland's survey on gender-based violence and intimate partner violence in Finland 2021). Over 50% of women and nearly 50% of men have experienced physical violence, threats or sexual violence, and of them, over 34% of women and nearly 20% of men from their current or former partner.

The philosopher Bernard-Henri Lévy, who has filmed a documentary in Ukraine about Russia's war of aggression against Ukraine, commented on the process in a recent interview (Helsingin Sanomat 15.7.2023). He points out that now it is time for philosophy to offer analysis. At the same time, he remarks that a philosopher travelling in a war zone offering comments on the situation is like a doctor, who only is treating the symptoms, but not curing the actual disorder. In psychiatry, we know that, in clinical practice, although sometimes treating the symptoms corresponds to the healing of the disorder, we also need a more profound and at least theoretical understanding of the origins and development of symptoms. For that, we need research and scientific discussion. Violence is a much wider concept than a psychiatric issue, but there are parts, in both the origins and effects of violence, that beyond doubt belong in the field of psychiatry.

In this volume, we publish an excellent conceptual overview of violence, especially the viewpoint about war, with a fascinating historical review by Professor Jyrki Korkeila, as an invited editor. The overview also illuminates the complexity of the ways humans justify violence. A violent and threatening environment can induce violence, but it also is possible that psychiatric problems lead to violent attacks. However, as Korkeila points out, it is more common that persons with psychiatric disorders are themselves victims of violence. Furthermore, besides the spectre of violence, especially persons with severe psychiatric disorders still face, in their everyday life, the stigmatization and discrimination that exacerbates marginalization and suffering.

Wars and other crises may force people to leave their home country and apply for safety in a foreign state. We need to increase our knowledge of the needs and appropriate care of refugees. In the current volume, we publish a review describing the needs and use of mental health and child protection services among children and youth with a refugee and migrant background (Kraav et al.). The authors identify obstacles in receiving suitable services, and point out the need for culturally competent service providers. As a solution, among others, an original study of Porta et al. highlights the importance of the inclusion of linguistic and cultural minorities in developmental projects related to services for immigrants. Castaneda et al. offers us a delightful and unique case study of an equine-facilitated therapy for a young, asylum-seeking girl with background of domestic violence.

In addition to articles on violence or trauma, we publish in this volume two inspiring studies of novel and promising treatment methods in psychiatry. One describes the method of using a virtual reality intervention among psychotic patients

(Mikkonen et al.), and the other reports the results of the observational pilot study of the Bergen 4-Day treatment for obsessive-compulsive disorder patients (Silver et al.). It is of utmost importance that we get knowledge of new methods in the Finnish context, and that we are able to share these experiences across the country and between different areas. Psychiatria Fennica offers a channel for that communication.

Finally, I return to the remark of Lévy that just curing the symptoms might not be enough. Psychiatry, operating in the areas of brain, mind and behaviour of humans, is located at the edge, where, among others, biology, sociology and philosophy meet. I am especially delighted that in many of the articles published in this volume the scope is larger than just medicine including, for example, child foster care, housing services and economic challenges. Although psychiatry cannot and should not take care of all aspects related to mental health, we must acknowledge them, and we should be able to give enlightened advice when needed.

Although our mini theme was gloomy, our warm editorial society, including Erika Jääskeläinen and Max Karukivi, made this process pleasant and inspiring. This is just a small example of how important social relationships are for our welfare. Everybody needs to belong to a society. For that, we should take care, not as psychiatric professionals, but as humans and citizens. Finally, I thank all the writers and referees for the excellent work you have done, for only with you, has this publication again been possible.

Tuula Kiesepää

Editor-in-Chief, Psychiatria Fennica



JYRKI KORKEILA

VIOLENCE AND WAR

KEYWORDS: PSYCHIATRY, VIOLENCE, WAR

Violence and war come in very different colours and contexts. The background factors for individual and group violence are to some extent shared and are to some extent operating on different levels. It is unfortunate that violence and war belong to humanity. New archaeological research has provided evidence that there has never been a “noble savage”, but that human beings have always had a certain propensity to individual and collective violent behaviour [1]. Considering our distant primate relatives, this is understandable and based on a vital ability for self-protection and gaining territories [2].

Clear and universal definition of violence is difficult due to the wide variety of moral codes in the versatile cultures of the world. What is acceptable and what is harmful are influenced by values and norms that are subject to continuous change. Who is defining violence and for what purpose defines the features of definitions. According to WHO violence is: “The intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation” [3]. Such a definition encompasses interpersonal, suicidal and collective violence. It is necessary to provide an internationally acceptable definition of violence for its prevention and legal regulation.

Intimate partner violence is a form of violence that alarmingly many parts of is not a punishable crime. A concept in English language, which is still common usage, “a rule of thumb” stems from the 17th century. According to folklore, it’s origin might be in allowing intimate partner violence with a stick that is not wider than a thumb. However, in Britain wife-beating had been prohibited for centuries, yet several court rulings in the United States in 19th century referred to this “ancient doctrine” [4]. To use this as a basis for rulings has been preposterous.

In the United States, approximately 1.5 million women and 834,700 men annually are raped and/or physically assaulted by an intimate partner. Women are more likely than men to be injured, sexually assaulted or murdered by an intimate partner. Studies suggest that one in four women is at lifetime risk [5]. The social restrictions during the Covid-19 pandemic increased considerably intimate partner violence. Therefore, intimate partner violence has been called the “pandemic within the pandemic” [6].

It wasn’t until early 1983 that Finland made physical punishment of a child illegal. Since the law came into force, the level of physically punished and level of murdered children have significantly decreased. Yet, pulling hair or ears, slapping and hitting with an object still occur in our country. Even severe forms of physical punishment still existed in a large population sample, as only 84% to 86% of children born in 1996 reported never being slapped or hit with an object [7]. Both intimate partner violence and childhood physical punishment have a considerable impact on mental health.

Homicide is defined as: “an unlawful death deliberately inflicted on one person by another person”. Annually more than 400 000 humans die by homicide, and the proportion of deaths ranges from 1 to 10%. In the most violent countries, the rate is up to 50 times higher than in some other countries. In many countries the rate has been declining for a long time. Suicide rate is 1.8-fold compared to homicide rate, but in some countries, homicide is one of the leading causes of death and in Latin America it is the leading cause of death among 15 to 49-year-olds. Twice as many people die by homicide than traffic accidents [8]. Psychiatric patients are more commonly the victims than perpetrators of violent crimes [9].

Collective violence as war has declined since 1945. Both the number of wars and people killed in wars have declined,

while the number of people killed due to terrorism has increased [8]. However, we may live in times when the level of collective violence has been lower than for many hundreds of years. The number of deaths, and especially population-based rates, during war were immensely higher during the period of warring states in the regions of modern China (488-403 BC) and Mongolian wars than ever since [10].

Violence has in early human history been a primary method of “setting things right”. The Hammurabi Code, around 1750 BC, was actually a major advancement at the time, because it was the first effort to regulate violence and prevent revenge done in blind rage. The law defined, e.g., how many cows the perpetrator had to give to the victim of robbery, and who was allowed to be killed in the event of foul play [11]. Western societies have the rule of law, but the sense of justice for citizens still incorporates to some extent a concept of “setting things right”. Legislature defines the consequence of different types of violent criminal behaviour by imposing costs, major restrictions of individual liberty or even death on a perpetrator.

Collective violence commonly encompasses the “setting things right” aspect. The leadership of a nation considers that its deserved demands have not been met. An example of this first type of collective violence is the First World War, when Germany’s leadership’s main motivation was to set things right with France after their defeat in the Franco-Prussian war of 1870 [12]. Therefore, an attack on France was deemed of utmost importance. Wars are often justified to citizens by somewhat hypocritical statements like the leaders of British Empire did in 1914: “we are defending democracy”. But Britain was allied with tsarist Russia, the most repressive state of Europe at the time. National self-interests dictate the motivations of entering a war, and this may lead to contradicting actions and motivations. In modern times, deliberation on what is the adequate self-interest worth for entering a war remains a topic of disagreement between strategists and historians.

Secondly, fighting for one’s form of government was one key motivation in the early 1790’s, when Russia, British Empire, Holy Roman Empire, Portugal and several smaller nations formed “the first alliance” to attack France in a joint effort to curb the spread of the French Revolution. This campaign was followed by a series of Napoleonic wars. At the time of these wars the British Empire fought with France in Northern America and Africa for the domination and colonization of territories [13]. In Northern America both sides were joined by native Americans that were very hostile to each other.

In addition to defending one’s form of government, nations are commonly motivated by defending or increasing the resources and territories they rule. There is an additional type of motivation for collective violence which has its roots in having experienced national shame due to some form of loss. This form of motivation of collective violence usually comprises a low level of rational consideration of costs and benefits. Both the Second World War and Russian war against Ukraine are examples of loss of national pride. All forms of motivation to war are overlapping, but the motivational background may be dominated by one of the types. Whether there are rational considerations or some form of deliberation relying on national myths, and to what extent, is the territory of historical studies.

Humans are emotional animals and recent cognitive science of decision making has shown that making inferences and conclusions is always guided by emotions. As Barbary Tversky argues, “emotion always comes first” [14]. But we can most often stop the enactment of our decisions, although they arise automatically from beyond our experienced conscious will. This points to the importance of learning how to contain our aggressive tendencies on an individual level and having international institutions for negotiating national disputes. According to Jonathan Glover such institutions might have well been the last resort in preventing the spin of controversies leading to the catastrophe in 1914 [15]. Anyhow, it is of importance to remember Immanuel Kant’s words: “Out of the crooked timber of humanity no straight thing was ever made”. His thinking has guided the modern concept of human dignity and is the basis of modern rule of law.

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References

1. LeBlanc S. Constant battles. The myth of the peaceful, noble savage. St Martin's Press. New York: New York, 2003.
2. Mitani J, Watts DP, Amsler SJ. Lethal intergroup aggression leads to territorial expansion in wild chimpanzees. *Curr Biol* 2010;20:R507-R08.
3. World Health Organization. World report on violence and health. Geneva: World Health Organization, 2002. Available at (accessed 21.6.2023) <https://apps.who.int/iris/bitstream/handle/10665/67403/a77019.pdf>
4. Rule of thumb. https://en.wikipedia.org/wiki/Rule_of_thumb, accessed 21.6.2023.
5. Cronholm PF, Fogarty CT, Ambuel B, Harrison SL. Intimate partner violence. *Am Fam Physician*. 2011 May 15;83:1165-72.
6. Moreira DN, Pinto da Costa M. The impact of the Covid-19 pandemic in the precipitation of intimate partner violence. *Int J Law Psychiatry* 2020 Jul-Aug;71:101606.
7. Österman K, Björkqvist K, Wahlbeck K. Twenty-eight years after the complete ban on the physical punishment of children in Finland: trends and psychosocial concomitants. *Aggress Behav*. 2014 Nov-Dec;40:568-81.
8. Our World in Data: Terms; Homicides, War and peace, and Terrorism. <https://ourworldindata.org/> accessed 21.6.2023
9. Soyka M, Graz C, Bottlender R, Dirschedl P et al. Clinical correlates of later violence and criminal offences in schizophrenia. *Schizophr Res*. 2007;94:89-98.
10. White M. Atrocitology. Humanity's deadliest achievements. Croydon: Canongate 2011.
11. Graber D. Debt. The first 5000 years. London: Melville House, 2011.
12. Hastings M. Catastrophe 1914: Europe Goes to War. London: Random House 2013.
13. French Revolutionary Wars. https://en.wikipedia.org/wiki/French_Revolutionary_Wars, accessed 21.6.2023
14. Tversky B. Mind in motion: how action shapes thought. New York: Basic Books, 2019.
15. Glover J. Humanity. A moral history of the twentieth century. London: Random House, 2000.



SIIRI-LIISI KRAAV, NATALIE JOUBERT, MERJA ANIS, JANET ANAND, MAILI MALIN,
MAX KARUKIVI, TOMMI TOLMUNEN

SCOPING REVIEW ON MENTAL HEALTH AND CHILD PROTECTIVE SERVICES OF MIGRATED AND REFUGEE CHILDREN AND YOUTH

ABSTRACT

One of the long-term consequences related to migration due to wars, violence, and ecological and climate crises is the additional challenges to the health and child welfare systems in the host country. Previous research has shown that the need for the help of migrant children and children of migrants differs from the help needs of the main population of the host country. In the current scoping review, our objective is to describe how the mental health and child protection services needs and use of child and youth refugees and migrants differ from those of the natives in the host country, and also to identify the main obstacles in receiving suitable mental health or child protective services. Implications for healthcare and child protective services are discussed.

KEYWORDS: REFUGEE, MIGRANT, MENTAL HEALTH, CHILD PROTECTION, OUT-OF-HOME CARE

INTRODUCTION

With the growing number of refugees and migrants worldwide, there is a growing need to understand the different challenges to the mental health of children and adolescents with a migrant background. It is essential to understand their specific needs relating to mental health and child protective services in order to create appropriate social and healthcare systems to address these needs. In Finland, there is very little research on mental health and child protection of migrant children. The few existing studies implicate the need for more research and the need to focus on developing more appropriate services for the diversifying population (1–3).

In this article, we use the concepts refugee and migrant to distinguish their different meanings (4). According to the 1951 Refugee Convention, a refugee is a person who is unable or unwilling to return to their country of origin owing to a significant fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion (5). It is possible to get refugee status either as a quota refugee or by seeking and getting asylum from the host country. An asylum seeker is a person who has fled their country of origin and is seeking international protection as a refugee but whose claim for refugee status has not yet been determined (6). Once the asylum claim has been accepted, they are called refugees (7). For refugees, the refusal of their request for asylum and return to their country of origin is likely to have dire consequences. Voluntary migrants, on the other hand, leave their home countries for different reasons, such as the wish to improve their lives by finding work, or in some cases for education, family reunion or other reasons. Their access to human rights is not necessarily threatened. In addition to adult refugees and families with children, an increasing number of refugee minors who are unaccompanied by their parents or carers seek asylum (8). By the terms first- and second-generation immigrant, we refer to people who are foreign-born or whose parents are born abroad, respectively. However, we emphasize that these concepts do not necessarily correspond to the identities of the people concerned (9).

Child and adolescent migrants are a heterogeneous group. Different studies may focus on children who arrive in the host country without their parents – as foreign-born adoptees whose parents are residents in the host country or unaccompanied refugee minors (URM, or asylum-seeking children) who have fled the adversities of their country of origin and arrived in the host country without their

parents or caregivers. Other studies focus on children and young people who arrive in the country with their parents and are not separated from their parents, that is, foreign-born immigrant children (i.e., 1.5 generation immigrant children (10)), and 2nd generation immigrants – born in the host country to immigrant parents. There are different threats to mental health and specific mental health and child protection service needs that are connected to each of these groups. However, the available research on most of these groups is still scarce.

Child and adolescent refugees, who account for more than half of the world's refugees, have a higher prevalence of mental disorders (PTSD, depression and anxiety being among the most reported) than children and adolescents of local populations in both high- and low-income countries (11). Migrant children who experience pre-migratory trauma due to events such as war, displacement or violence, face unique challenges that can significantly impact their mental health and wellbeing. Additionally, they may have experienced the loss of social support networks, including family, friends and community ties, due to displacement (7). In addition to pre-migratory trauma, migrant children often also face peri- and post-migratory adversities that may increase their mental health concerns (12–14). Racism and discrimination that many refugees and migrants experience in the new country cause stress (12) and these experiences of discrimination correlate significantly with worse health outcomes and lower quality of life (15,16).

Migrant children may be in heightened need for child protective services compared to their non-migrant peers. Studies from Finland, Sweden and Norway have indicated that immigrant children and youth are more likely to enter out-of-home care than children of the host country's population (3,9,17–20). On average, immigrant families have more welfare risks than the host population. For example, in Finland child family poverty is significantly more common in families with a migrant background than the host population (21). Children with a refugee background also experience more stressful events in their new home country, for example, bullying and anxiety at school, than average during their lives (22,23). Acculturation stress that families face in adjusting to their new home country has been recognized as a risk factor for family-related violence in refugee families, especially in relatively new immigrants (24,25). It has been suggested that getting settled into a new environment and learning about Western child-rearing practices and laws may in time decrease physical discipline practices (24). In a cohort study, parental trauma history and PTSD were associated with

harsh parenting styles (26). In order for refugee children to recover from their pre-migration negative experiences and avoid the negative effects of transgenerational trauma as well as additional post-migration traumatization, it is important to make treatment of traumatized children and their families early and easily available upon arrival in the host country (27). The host country needs to use a trauma-informed and culturally sensitive approach to provide social and health services to immigrant children and young people (7).

The current article was born in cooperation between two projects: “Co-research and co-creation of child welfare social work and adolescent psychiatry” (LANUPS) and “Child protection expertise in social work with immigrant children and families (LAMPE). In the LANUPS project, the focus was on young people who needed both mental health services and child protective services, whereas in the LAMPE project, the focus was on social work with immigrant children and families. Therefore, we were interested in previous research on migrant children and youth and their mental health challenges and child protective service needs.

In this scoping review, we aim to present research results concerning the mental health and child protection services need and use of children and youth who have migrated to another country or were born to a migrated family. Due to the limited availability of prevalence studies on the topic, we included review articles and editorials in which the topic was covered. Since the included studies mainly focus on mental health perspectives and the child protection service aspects are very limited, the main emphasis in this review is on the mental health services of children, and child protection issues are more as a context to the analysis (21,22).

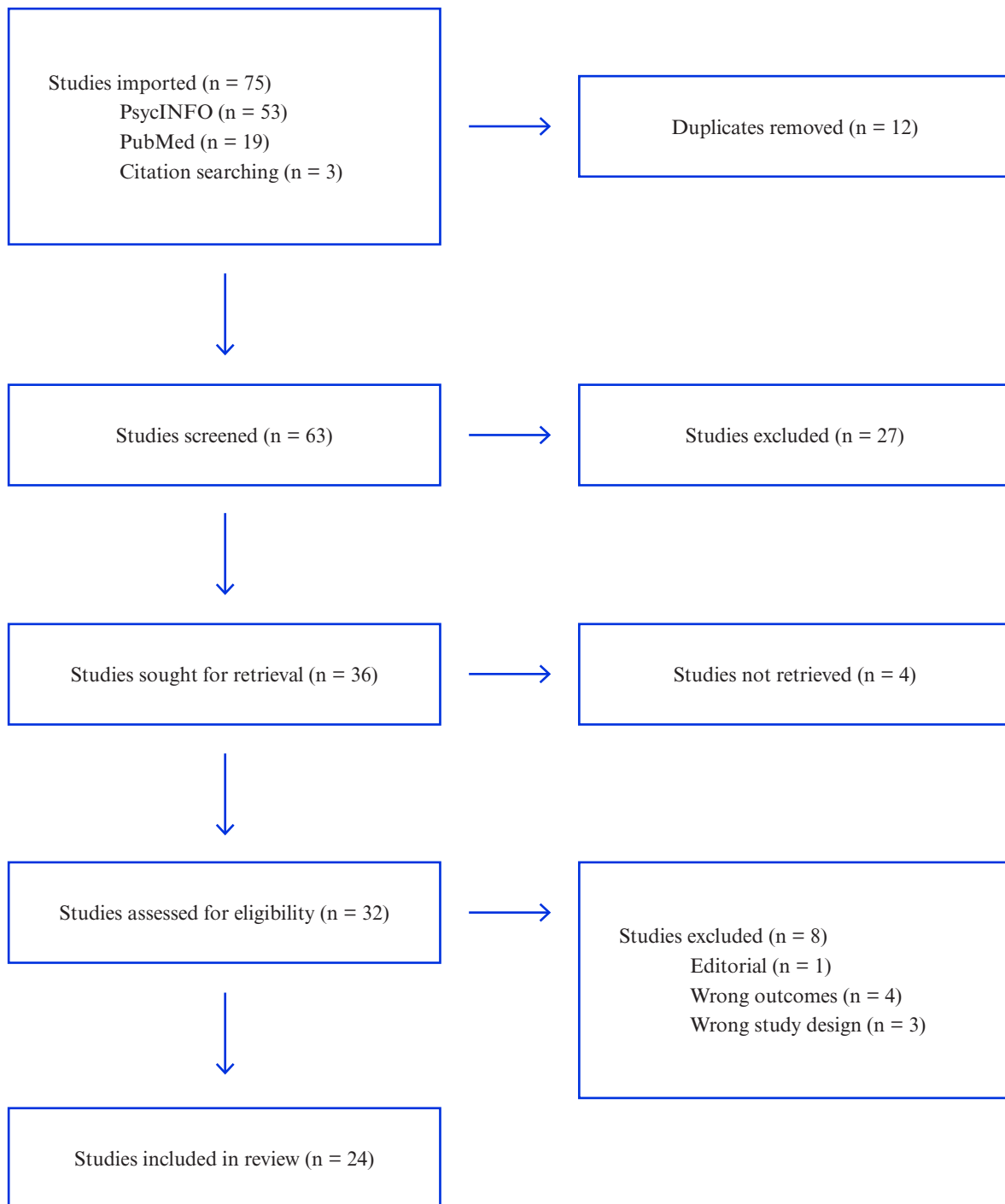
Focusing on migrant and refugee children and comparing this diverse group to the host population causes methodological, and also ethical, issues for the study. The review concerns both first- and second-generation immigrants, refugees, and asylum-seeking children and youth. Migrants/immigrants as a group is very heterogeneous, and the services and service systems that support them vary according to the host country and society. Comparative research settings and results may strengthen stereotypes and prejudices if the interpretations do not consider ethical aspects. We are aware of these concerns and aim to apply ethically sensitive ways of interpreting and writing the results (3,9,28). Reviewing research internationally can produce knowledge for developing services in the Finnish context.

METHODS

The aim of the current review is to present research results concerning the mental health and child protection services use of children and youth who have migrated to another country or were born to a migrated family. In March 2023, we searched the electronic databases PsychINFO and PubMed for peer-reviewed journal articles written in English using the following search terms: (refugee* OR "asylum seeker*" OR displace* OR migrant* OR immigrant* OR "asylum-seek*" OR "displaced child*" OR "resettlement country") AND ("mental health" OR "mental illness" OR "mental disorder" OR psychiatric) AND ("foster care" OR "out of home care" OR "foster group care" OR "adopted child*" OR "child protective services"). The search was conducted within the titles and abstracts in each database. Additional filters were used to limit the results by age: in PsycINFO 0-29 years (childhood, adolescence, young adulthood), and in PubMed 0-24 years (childbirth to 18 years, and young adult 19-24 years).

Seventy-two studies were found in the databases and imported to the Covidence program. 12 duplicates were removed. Additionally, references to the articles were searched, and in this way three additional articles were added to the screening. All entries were screened by two researchers and conflicts were discussed before making a final decision. After screening 63 abstracts, 27 studies were found irrelevant, and 36 full-text studies were assessed for eligibility. Finally, 24 studies were included in the review (*Figure 1*).

Figure 1. PRISMA flow chart of the review process



RESULTS

Twenty-four full-text articles were included in this review. These included sixteen original research articles, seven reviews and one column. The oldest of the articles were two original research articles from 2004 and the newest two reviews from 2022. Most of the studies were conducted

in the USA and UK and the target groups varied in the different studies. The studies in this review focus mainly on migrants/immigrants or refugees, but research concerning asylum-seeking children is also included. The full list of articles included, with their main contribution to our research question are listed in *Table 1*.

Table 1. The articles included, with their main contribution to the research questions

1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
Bronstein	2012	Original research. Cross-sectional	UK	PTSD in asylum-seeking Afghan children (N=222, male, age 13–18 years, separated from parents).	1/3 had PTSD. Cumulative trauma predicted PTSD. Semi-independent or independent accommodation is associated with higher level of symptoms than foster care.
Detlaff	2010	Original research. Cross-sectional (with a retrospective component)	USA	Latino children of immigrant parents (N=430, age 2–14 years) vs native parents in U.S. based on NSCAW survey. Analyses were based solely on children living with biological parents at the time of the baseline interview.	Latino preschool-aged children of immigrant parents have more mental health service needs (based on Child Behavior Checklist) than children of U.S.-born Latinos. Latino children of immigrants have more mental health services (based on data gathered from caregivers) and less unmet mental health needs (estimated by the percentage of youth who demonstrated a clinical need for mental health services but had not received any during last year) than children of U.S.-born Latinos.
Finno-Velasquez	2016	Original research. Prospective	USA	Mental health and service use of Latino children who remained in home after child maltreatment investigation (N=390, age birth–17.5 years, mean 8.48 years). NSCAW II survey.	Compared to children whose parents were U.S. citizens, children of undocumented immigrant parents received less mental health services. There were no significant differences between the groups in mental health service needs.



1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
Geltman	2008	Original research. Descriptive survey	USA	Effectiveness of mental health counselling and health services on functional health outcomes among Sudanese refugee minors in USA foster care (N=304, 84% of the sample were male, mean age 17.6 years).	45% of minors received counselling. Counselling was not associated with health outcomes. The majority of participants, especially those with PTSD, sought medical care for symptoms associated with emotional or behavioural problems.
Grumi	2017	Original research	Italy	Comparison of social records of Italian (N=153) and immigrant families (N=175) referred to CPS for child maltreatment. The study concerned 328 minors (48.8% male, mean age 8.41 years, range 0-17).	In prevalence of child maltreatment there were no differences in Italian and migrant families. Immigrants approved violence and punishments and suffered from low SES. In Italian families were more distal and proximal risk factors.
Horn	2017	Original research, register-based	USA	Experiences of Somali and Oromo youth who attended public school between 2008–2011 (early childhood education to grade 12) and were involved in Minnesota's child protection system (CPS) between 2000 and 2013. (N=691, 53.4% male).	Somali and Oromo youth were involved in CPS at low rates (3.7%). Caregivers whose children were in CPS need social support and mental health/coping support and parenting skills. According to CPS workers Somali and Oromo youth and their caregivers had significant mental health needs. For out-of-home placements relative foster care was used infrequently, whereas they were often placed into restrictive forms of out-of-home placement.
Huemer	2016	Observational	Austria	A retrospective analysis (2001-2007) of clientele in a clinic offering short-term trauma therapy. (N=2510, age range 1-17 years, 50% male).	In the first years only about 10% of the clientele were immigrants, whereas in 2007 20% of the patients were immigrants and children of immigrants.



1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
Leavey	2004	Original research. Cross-sectional	UK	Strengths and Difficulties Questionnaire scores' association with sociodemographic variables including language preference in a London school. (N=329, age mean 13.2 years, 59.9% male).	Migrant and refugee children had higher level of psychological distress on the Strengths and Difficulties Questionnaire than their non-migrant peers. Young migrant boys had more emotional difficulties than their UK-born peers, but fewer conduct and hyperactivity problems.
Luster	2010	Original research. Qualitative	USA	Factors supporting or hindering positive adaptation over the long term (seven years) after resettlement in USA. Interviews with Sudanese URM (N=19, mean age 22 years, 17 of 19 male) and their foster parents (N=15 foster families).	Foster parents and youth agreed on education and work as key indicators of success. For youth it was important to help those left behind, whereas foster parents saw this obligation sometimes problematic. Foster parents talked more than youth about mental health problems as risk factors for successful adaptation.
Pedrini	2015	Original research. Observational study	Italy	Analysis of access patterns and care pathways at first-time contact at child and adolescent mental health services (N=399, mean age 10.5, 56.9% male).	Compared to Italian children, children of immigrant families were more often referred to children and adolescent mental health services by teachers rather than parents. Causes may be related to language or social inclusion issues.
Rajendran	2010	Original research. Observational study	USA	Analysis of family service use by immigrant families in the U.S. child welfare system. (N=312, families, age of children 2–15 years, 44% male). NASCAW survey.	Child-related factors for greater use of family support services were higher levels of internalizing and externalizing problems, as well as experiences of neglect. Caregiver-related factors included mental health problems, history of arrests and prior reports of maltreatment. Caseworker-related factors were training on cultural issues, and perception of organization's problems.



1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
Rousseau	2013	Original research. Case study	Canada	Through three cases (a young boy, a 6-year-old boy, a 7-year-old girl), the collaborative care model in mental health is described and analysed. Emphases on trauma awareness.	Helping refugee children whose families have experienced trauma requires a combination of cultural knowledge and trauma therapy. Primary care institutions that are very close to the family living environment may be appropriate to help establish a support network.
Sirriyeh	2018	Original research	UK and Ireland	The role of foster care in helping unaccompanied asylum-seeking young people's transitions to adulthood (N=23 foster carers and N=21 URM from England, age range 13-18 years, all male; N=16 foster carers and N=21 URM from Ireland, average age 15.8 years, 13 of them male).	After leaving foster care the impact of the care and the relationships with foster parents will endure. Providing foster carers training in emotional, legal and social recognition (Honneth's theory of recognition) will help build self-confidence, self-respect and self-esteem in URM as they transition into adulthood.
Tan	2016	Original research	USA	Incidence of emotional and behavioural disorders in immigrant children. The study included 1.5 generation immigrants (N=1378, mean age 11.2 years), 2nd generation immigrants (N=4194, mean age 8.4), foreign adoptees (N=270, mean age 10.7) and non-immigrants (N=54877, mean age 9.5).	Odds for having ADD/ADHD, conduct disorder, anxiety or depression were the lowest for 1.5 generation immigrant children, followed by 2nd generation and the highest in non-immigrant children. Connection to heritage culture may explain the lower rates of mental disorders in recent immigrants.
Thomas	2004	Original research. Qualitative	UK	Pre-flight experiences of unaccompanied asylum-seeking children (UASC) (N=100, 59% male, mean age 15).	UASC have different traumatic experiences and there is a need for culturally appropriate research methods to identify their health and social needs after arrival and to develop and improve the services.
Tordön	2019	Original research. Cross-sectional questionnaire	Sweden	Highschool students in out-of-home care (OOHC) were compared to students not in OOHC (N=5839 students, mean age 17.97, 44.6% male).	Being an immigrant and having parents born abroad was more common in OOHC group than in non-OOHC group.



1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
Abraham	2019	Review	USA	Review of epidemiology, risk and protective factors associated with youth suicide, and global strategies to address it.	Refugee, immigrant, and indigenous youth as well as those in foster care or homeless are more vulnerable and at increased risk for youth suicide.
Fledderjohann	2021	Review	UK	Review included original research articles, based on UK data that focused on mental health in children and young people.	Compared to UK-born peers, migrant children and young people, especially younger boys scored lower for conduct problems and higher for emotional and peer problems. In 14-16-year-olds conduct problems were more prevalent than in UK-born peers. In immigrant detention centres extremely high levels of depression and anxiety. Inconsistent findings regarding ADHD.
Gao	2022	Systematic review and meta-analysis	China	The relationship between migration status and risk of autism spectrum disorder (ASD) and attention-deficit-hyperactivity disorder (ADHD).	Migration was associated with increased risk for ASD. No association was found between migration and ADHD or hyperactivity.
Hornfeck	2022	Scoping review	Germany	Effects of asylum process on mental health.	Refusal of asylum had a negative effect on the wellbeing due to instability and fear of return. Rather than asylum process or status per se, the instability and uncertainty affect the wellbeing of young refugees. Maternal migration was a risk factor of ASD, and it was likely for migrant children to have ASD comorbid with intellectual disability.
Mitra	2019	Systematic review	UK	Prevention of psychological distress and promotion of resilience amongst Unaccompanied Refugee Minors in resettlement countries.	URMs are less likely than accompanied immigrant children to receive mental health services. CBT was found beneficial to PTSD. Those living in foster care had lower depression and PTSD symptoms than those in independent care arrangements. Living reception settings that restricted freedom was connected to more anxiety.



1st author	Year	Type of article	Country	Context, participants' age.	Results of the research questions.
O'Higgins	2018	Systematic review and meta-analysis	UK	Impact of placement type on educational and health outcomes in unaccompanied refugee minors.	Eight studies focused on accommodation type and mental health outcomes. Results suggested that foster care and placements that are culturally sensitive are associated with better mental health outcomes.
Seeman	2020	Review	Canada	Comparison of psychosis risk in immigrants and adoptees.	The risks of mental health in immigrants and adoptees are similar. Being exposed to one's ethnic and age peers who share a similar background may protect against the incidence of psychosis in immigrants and adoptees.
Murray	2018	Column	USA	Description of the effects of toxic stress in child refugees.	Prevention of toxic stress in child refugees should be the main goal of healthcare services in the receiving country. Efforts should be made to address caregiver stress and improve their ability to provide safe, reliable and nurturing care.

Abbreviations: ADD – attention deficit disorder; ADHD – attention-deficit hyperactivity disorder; ASD – autism spectrum disorder; CPS – child protective services; NSCAW – National Survey of Child and Adolescent Well-being; OCH – out of home care; PTSD – post-traumatic stress disorder; URM – Unaccompanied refugee minors

MENTAL HEALTH PROBLEMS OF MIGRANT AND REFUGEE CHILDREN AND ADOLESCENTS COMPARED TO THEIR HOST COUNTRY-BORN PEERS

There are contrasting results regarding the mental health needs of migrants compared to their non-migrant peers. In the articles included in this scoping review, there were several studies and reviews emphasizing the increased mental health issues in refugee and migrant children and adolescents. In a UK sample of asylum-seeking minors from Afghanistan, over a third of study participants had post-traumatic stress disorder (PTSD), and cumulative trauma was associated with higher PTSD scores (29). In the first school-based study to compare the emotional and behavioural problems of migrant and refugee children with those of their UK-born peers, Leavey et al. (2004) found that migrant boys and younger migrant children exhibited significantly higher levels of emotional symptoms than their UK-born counterparts (30). In an American study,

preschool-aged Latino children of immigrant parents were found twice as likely to score in the clinical range of the child behaviour checklist than Latino children of U.S.-born parents (31). A review article focusing on the relationship between migration status and the risk of autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) found that maternal migration is a risk factor for ASD, and migrant ASD children are more likely to have a comorbid intellectual disability. The role of migration on ADHD remains controversial, more studies are needed to assess the association between migration status and ADHD (32). Seeman (2020) analysed the reasons why immigrant status can be associated with an increased risk of psychosis: experiencing trauma, difficulties in assimilating into the new family or country and identity questions. Abraham and Sher (2019) recognized, in their review article concerning the epidemiology of risk and protective factors of youth suicide, immigrants and refugees as a vulnerable group who are at a higher risk of suicide. Furthermore, living

in foster care or homelessness increased the risk of youth suicide, indicating an even higher risk for immigrant or refugee youths who are separated from their parents (34). Survivor guilt was apparent in the record of several suicide attempts of one Sudanese unaccompanied refugee minor, who was traumatized by experiences on his way from Sudan to the U.S. (35).

On the other hand, in some respects, immigrant children seemed to cope better than non-immigrants or equally well. Tan (2016) compared four different groups of children: non-immigrant children, foreign adoptees (whose adoptive parents were U.S.-born Americans), 1.5 generation immigrant children (children who have migrated with their parents) and 2nd generation immigrant children. They found that the prevalence of ADD/ADHD, conduct disorder, anxiety and depression was the highest in foreign adoptees, followed by non-immigrant children. Both 1.5 and 2nd generation children had a low prevalence of the four mental disorders. Additionally, Leavey and colleagues found that migrant and refugee children had higher pro-social behaviour scores and fewer conduct and hyperactivity problems, and they were less likely to use alcohol than their UK-born peers (30). Finally, among U.S. child welfare clients there were no differences in mental health between children of Latino immigrants and children of U.S.-born parents (31,36).

CONSIDERING EFFECTS OF TRAUMA ON MIGRANT OR REFUGEE CHILDREN'S WELLBEING

Refugees often experience significant traumatic events, that may happen not only before leaving the country of origin but also during the migration process and after that. Among the reasons why unaccompanied asylum-seeking children have fled their country of origin are: the death of parents, the disappearance or imprisonment of family members; persecution on the grounds of ethnicity, religion or sexuality; forced recruitment into rebel factions, and armed conflict (37). In his column, Murray (2018) warns against the toxic stress caused by accumulating adverse childhood experiences that child refugees face. Toxic stress is defined as exposure to extreme, frequent and persistent adverse events without the presence of a supportive caretaker (39). Toxic stress results in biological alterations, which affects the nervous, endocrine and immune systems, and can extend well into adulthood (38).

Sometimes, refugee minors are not willing or able to verbalize their traumatic experiences and seek help for

mental reasons. In these circumstances, the symptoms may present in different ways. Geltman and colleagues (2008) found that among Sudanese minors, who arrived in the U.S. unaccompanied, there were high levels of help-seeking for health problems and symptoms that may be consistent with somatization, especially among those with PTSD (40). Foster parents of the so-called 'lost boys of Sudan', unaccompanied minors who resettled in the USA, on average prior to their 18th birthday, described in interviews the effects of trauma and adversity being the reason for excessive alcohol consumption among those 'lost boys' who did not to succeed in adapting to American culture (35). Seeking help because of somatization problems from general healthcare providers was associated with worse functional and behavioural health (40).

Huemer and colleagues (2016) analysed the clientele and service utilization of the low-threshold, short-term trauma therapy clinic "The Buoy" in Austria during the first six years (2001-2007) of the clinic's existence. They noticed that compared to locals, it took longer for the immigrant children and young people to find their way to the clinic. During the first years only around 10% of all patients were immigrants, the utilization rates of immigrants rose throughout the observation period to 20% in 2007. There is a paucity of information about specific barriers that prevent service utilization by immigrants. According to Rousseau (2013), it is important to understand cultural factors and incorporate trauma therapy methods when working with refugee children and families – a comprehensive approach that considers individual, familial and social aspects is required for effective treatment and support. Notably, Bronstein and colleagues (2012) noticed that those unaccompanied asylum-seeking children placed in foster care rather than in independent or semi-independent accommodation had lower levels of PTSD.

DIFFERENCES IN CHILD PROTECTION SERVICE UTILIZATION BETWEEN REFUGEES OR MIGRANTS AND THEIR NON-MIGRANT PEERS

In addition to differences in mental health and healthcare needs between migrant and non-migrant children and youth, migrant families also have different patterns of utilizing child protection services due to cultural and socioeconomic differences. Dettlaff and Cardoso (2010) and Dettlaff et al. (2009) pointed out that there are significant differences in the risk factors and type of maltreatment experienced by Latino children of immigrants when compared to children of U.S.-born parents. Grumi et al. (2017) compared the Italian and immigrant families' records

of child protective services (CPS) from 2004–2016. They found that two different patterns of factors characterize Italian and foreign cases: immigrant families seem to suffer more from low socioeconomic status and have more positive attitudes concerning corporal punishment, whereas Italian families have more distal (experience of neglect or violence in parent childhood) and proximal (parent psychopathology, problematic relationship with family of origin) risk factors. There were no differences in typologies of maltreatment between Italian and immigrant families. The most relevant factor that affected the CPS workers' placement decisions for both Italian and immigrant parents was "lack of knowledge or interest relating to child development". This factor increased the odds of child removal from immigrant parents by 205% and from Italian parents by 2931%.

OBSTACLES IN PROVIDING ADEQUATE SERVICES TO MIGRANTS AND REFUGEES

In the National Survey of Child and Adolescent Well-Being (NSCAW) study, a surprising difference was found relating to the mental health service utilization by children of Latino immigrants compared to children of U.S.-born Latinos. The children of immigrants had higher mental health needs (indicated by the scores of the Child Behavior Checklist) and they were also more likely to receive mental health services and, therefore, less likely to have unmet mental health needs compared to children of U.S.-born Latinos (31). This difference could be attributed to immigrants' children being exposed to the social service system, or a result of U.S.-born Latinos having previous negative experiences with the mental health system due to a lack of culturally competent service providers (31). In another U.S. study, immigrant families of Black non-Hispanic children and families with Hispanic children used fewer services compared to immigrant families of White non-Hispanic children (42). These findings underline the lower rates of service access by minorities. In Italy, immigrant children are most often referred by teachers for first-time consultations at child and adolescent mental health services, which may be partly caused by language-related difficulties, social inclusion issues, or that parents belonging to minority ethnic groups have limited information about the function of mental health services (43).

Importantly for the case of the 'lost boys' of Sudan, the

reported receipt of mental health counselling had neither a positive nor negative association with health outcomes (40). However, refugees and asylum seekers may be particularly anxious about personal information affecting their legal status, leading to a lack of trust in mental health providers (34). Even if children of immigrants are citizens themselves, parental immigration status can serve as a barrier to accessing services (31). Finno-Velasquez and colleagues (2016) used the data of the NSCAW II study to compare the mental health service needs and utilization in child protection clients based on their parent's immigration status. In their study, a gap between overall clinical need and service receipt was identified only for children with undocumented parents.

One consideration when creating or improving systems to help immigrants adjust to their new country is sensitivity to cultural differences regarding beliefs about mental disorders and respective mental health services. Whilst unaccompanied minors from Sudan appreciated the advice and support they received from their foster parents or caseworkers, they were unwilling to engage in counselling. They believed people who get counselling to be "crazy, mental" (35). Rajendran and Chemtob (2010) found that cultural issues and concerns with bureaucracy may influence the utilization of social services by immigrant families. Caseworkers who receive training in cultural issues are more likely to support and address the unique needs of immigrants, leading to increased service use. However, concerns with bureaucracy and rigid adherence to rules and regulations may pose barriers for immigrants in accessing and navigating social services effectively. Furthermore, healthcare practitioners should consider screening and providing extra resources for migrant children (32).

DISCUSSION

The chief result of our scoping review is that migrant children and young people are a heterogeneous group and that there are conflicting results regarding their mental health status and needs. Articles included in this review identified several barriers that hinder optimal mental health and child protection services provision for refugees, asylum-seekers and other immigrants. The need for culturally competent service providers and trauma-aware services has been emphasized.

The initial research question for this review rose from our work with children and adolescents who need both child protective services and mental health services at the same

time. Therefore, we searched for articles that mentioned both mental health and child protective services in migrant children and youth. There were only a few articles that focused on both of our topics of interest simultaneously. In the majority of articles the focus was on mental health and in only a few also on child protection. Therefore, in the current review we have the child protection aspect mainly as a context to mental health issues.

COMPARISON WITH PREVIOUS LITERATURE

The “immigrant paradox” has mostly been described in the physical health of first-generation immigrants who initially have health advantages over their local counterparts, but the more immigrants get assimilated into the social and cultural norms, the more their health status resembles the locals' (44,45). Even though the same effect has been less prevalent in the studies of migrants' mental health, it has been suggested that it may partially explain the conflicting results concerning the mental health issues in immigrants and non-immigrants and why foreign-born immigrant children often outperform their non-immigrant counterparts on a variety of outcome measures (10). According to the “immigrant paradox” phenomenon, recently arrived immigrants do better in mental health outcomes than their non-immigrant peers in the host country (46). These advantages typically dissipate after living in the host country for several years (47) and in future generations (10). The explanation for the “immigrant paradox” remains unclear. A possible reason why immigrant children, according to some studies, do seemingly better than their non-immigrant peers may be cultural or caused by the family's pre-, peri- and post-migration experiences. According to Leavey and colleagues (2004), psychological distress in migrant and refugee children might be experienced by the child internally as emotional difficulties that they are unable to process or resolve through outward displays of anger and aggression. Tan (2016) suggests that the likely cause of foreign-born and U.S.-born immigrant children's better adjustment compared with the foreign adoptees lies in the congruency between a child's genetic predisposition and the US culture. Having a family who provides a connection to their heritage culture serves as a protective mechanism against emotional and behavioural problems (10).

Another thing that stood out from our selection of articles, compared to previous literature regarding migrant mental health, is that only one study in our search results mentioned increased risk of psychosis (48). Risk of non-

affective psychosis in refugees and migrants has been studied extensively, and noted consistently throughout different studies (49–51). A meta-analysis combining data of nine studies from Scandinavia and Canada concluded that the risk of the manifestation of schizophrenia and associated non-affective psychoses is statistically significantly increased in refugees compared with the native population as well as compared with non-refugee migrants (52). A Dutch study comparing prevalence of psychotic experiences in majority and minority general population adolescents found that prevalence of psychotic experiences was associated with perceived personal discrimination, and a weak ethnic identity (marginalization and assimilation) (53).

THE BARRIERS FOR UTILIZING MENTAL HEALTH AND CHILD PROTECTIVE SERVICES

The barriers to mental health and child protective services utilization could be described from three different perspectives. Firstly, barriers related to migrant children and their families. An important consideration is the cultural differences in the attitudes toward having psychiatric symptoms that may pertain to migrants. For many, it may be considered too humiliating to admit or not acknowledged as a problem at all. A qualitative study brought out that a concern of stigma related to the child's “madness” inhibited British Asian parents from seeking help from mental health professionals (54). Bradby and colleagues (2007) described three ways in which Asian parents were resisting the “stigma of madness”: 1) whenever possible parents prefer to frame their child's problems as a behaviour (naughty, immature), not an illness; 2) if the mental illness was serious, persistent or was obvious, parents tried to minimize gossip by insisting that it is a particular and limited deficit or that their child had problems previously, but had been cured now; 3) the most extreme strategy adopted by migrant parents in order to avoid gossip was to remain beyond the reach of service provision. On the other hand, Luster et al. (2010) conducted in-depth interviews with Sudanese unaccompanied asylum-seeking minors and their foster parents. They noticed that foster parents often saw mental health problems (psychosomatic symptoms, fits of rage, substance abuse or psychosis) as a significant problem in adaptation, whereas migrant youth

had a different view, seldom mentioning mental health problems, and not readily accepting counselling. It is also possible that migrant parents and youth experience 'othering' in many encounters in the new host society, and as a consequence they want to emphasize their ordinariness and respectability instead of revealing possible difficulties and the need for health and social services (55,56).

Secondly, barriers to mental health services utilization may be related to service providers. The host country may lack culturally sensitive and knowledgeable specialists to treat and support migrant children and youth. For example, culturally sensitive trauma therapy and trauma-informed social work is of utmost importance in creating social and health services for immigrants (7). Thus, if caseworkers and foster parents were provided with an opportunity for higher education in counselling and mental health help, it could be easier to provide some support to those immigrants who are hesitant in accepting help for fear of stigmatization. There may also be a lack of culturally or linguistically appropriate resources to help migrant communities (57). As noted by Dettlaff and Cardoso, (2010), 2nd generation immigrants may have lower levels of help-seeking because they have prior negative experiences with the mental health system where culturally competent service providers are lacking. The inability to communicate in the local language is a major barrier to accessing and remaining in healthcare, including mental healthcare (45,58,59). Also, the Finnish research on the health and welfare of adult immigrants (60) emphasizes the importance of improving the mental healthcare services for immigrants, because the use of services is significantly low in comparison to the need of those services. Severe depression and anxiety symptoms of studied immigrants were as common as in the host population, but the use of mental health services was a lot lower. Finnish studies also indicate that the early intervention services do not meet the needs of immigrant families and children, since out-of-home care placements more often concern children with an immigrant background than children with Finnish origin (3,9).

Finally, there may be structural barriers to mental health services utilization. Structural inequalities, such as poverty, unemployment, discrimination and experiences of temporality and everyday insecurity, which may lead to societal marginalization, concern immigrant families more than the host population (61). Service systems and practices which do not take into account multilingual and culturally diverse populations can also build structural barriers hindering access to services (1). Lack of a supportive network

is more common in immigrant families than in majority population (41). Resettling organizations and community-based resources have been found to be an effective way of buffering toxic stress in child refugees (38). As was proposed in the review article by Abraham and Sher (2019), providing more social support for refugee youth, as well as promoting the socioeconomic wellbeing of immigrants and refugees may be effective in improving mental health in these groups.

CONCLUSIONS

Our article presents a rather small number of studies on a variety of topics, and therefore the conclusions are suggestive, and the recommendations remain very general. However, our scoping review is in agreement with other authors – differences in mental health issues and mental health and child protection services needs and use comparing migrant and non-migrant children and adolescents in a particular country is a topic that needs more research. Additionally, research is needed to determine if parents of different immigration status (recent immigrants vs non-immigrants) might have different concepts of mental health problems in children (10), or to what extent do the attitudes change when a family lives in their new country for a longer period of time. Longitudinal studies are required in addressing unaccompanied refugee minors and examining how they develop and change from the beginning of placements, through the leaving care stage and into adulthood (62). Furthermore, research is needed to investigate how parents of children with different backgrounds (foreign adoptees, non-immigrant, immigrant, refugees and asylum seekers) perceive mental health and other welfare issues and their help-seeking behaviours on behalf of their children (10). Research on child welfare and especially child protection services concerning migrants is very limited according to our literature search, and needs more focus in the future.

The current research emphasizes the importance of building culturally appropriate support for those immigrants experiencing mental health problems. To avoid or mitigate toxic stress in child refugees, early intervention is essential to improve the child's environment and help children build resilience and provide care based on the most recent evidence.

Further research is needed particularly in the context of the Finnish society and service system to explore and understand the specific cultural obstacles faced by immigrants and to develop strategies that mitigate bureaucratic challenges,

thereby promoting better service provision and utilization among diverse immigrant populations.

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References

1. Anis M, Turtiainen K. Social Workers' Reflections on Forced Migration and Cultural Diversity—Towards Anti-Oppressive Expertise in Child and Family Social Work. *Soc Sci* [Internet]. 2021 Feb 25 [cited 2023 Aug 22];10(3):79. Available from: <https://www.mdpi.com/2076-0760/10/3/79>
2. Kestilä L, Karvonen S, Aalto AM. *Suomalaisten hyvinvointi 2018*. Helsinki: Terveyden ja hyvinvoinnin laitos; 2019. (Teema, 31).
3. Kääriälä, Antti; Keski-Säntti, Markus; Aaltonen, Mikko; Haikkola, Lotta; Huotari, Tiina; Ilmakunnas, Ilari; Juutinen, Aapo; Kiilakoski, Tomi; Merikukka, Marko; Pekkarinen, Elina; Rask, Shadia; Ristikari, Tiina; Salo, Jarmo; Gissler, Mika. Suomi seuraavan sukupolven kasvuympäristönä : Seuranta Suomessa vuonna 1997 syntyneistä lapsista, joilla on ulkomailla syntynyt vanhempi [Internet]. Helsinki: THL; 2020. Available from: <https://www.julkari.fi/handle/10024/140741>
4. UN General Assembly. New York Declaration for Refugees and Migrants : resolution / adopted by the General Assembly [Internet]. 2016 [cited 2023 Jun 28]. Available from: <https://www.refworld.org/docid/57ceb74a4.htm>
5. United Nations. *Convention Relating to the Status of Refugees*. Swizerland: United Nations; 1951.
6. United Nations. *Universal Declaration of Human Rights*. Adopted by the United Nations General Assembly on 10 December 1948. Article 14. [Internet]. 1948 [cited 2023 Jun 23]. Available from: <https://www.ohchr.org/en/human-rights/universal-declaration/universal-declaration-human-rights/about-universal-declaration-human-rights-translation-project>
7. Rousseau C, Measham T, Nadeau L. Addressing trauma in collaborative mental health care for refugee children. *Clin Child Psychol Psychiatry* [Internet]. 2013;18(1):121–36. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2013-01781-009&site=ehost-live&cc=rousseau@mcgill.ca>
8. Hornfeck F, Sowade C, Bovenschen I. Effects of the asylum process on the mental health of unaccompanied young refugees—A scoping review. *Child Youth Serv Rev* [Internet]. 2022;137. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2022-57754-001&site=ehost-live&ORCID=0000-0002-3436-3673hornfeck@dji.de>
9. Anis M, Malin M. Ulkomaalaistaustaiset lapset ja nuoret lastensuojelun sijaishuollossa: sijoitusten määrän, perusteen ja sijoituspaikan tarkastelu vuosina 1991-2015. *Janus Sos Ja Sos Tutkimuksen Aikakauslehti* [Internet]. 2023 Mar 2 [cited 2023 Jun 28];31(1):4–23. Available from: <https://journal.fi/janus/article/view/115427>
10. Tan TX. Emotional and behavioral disorders in 15th generation, 2nd generation immigrant children, and foreign adoptees. *J Immigr Minor Health* [Internet]. 2016;18(5):957–65. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2016-38255-005&site=ehost-live&ORCID=0000-0001-9496-3470tan@usf.edu>
11. Frounfelker RL, Miconi D, Farrar J, Brooks MA, Rousseau C, Betancourt TS. Mental Health of Refugee Children and Youth: Epidemiology, Interventions, and Future Directions. *Annu Rev Public Health* [Internet]. 2020 Apr 2 [cited 2023 Jun 22];41(1):159–76. Available from: <https://www.annualreviews.org/doi/10.1146/annurev-publhealth-040119-094230>
12. Eruyar S, Huemer J, Vostanis P. Review: How should child mental health services respond to the refugee crisis? *Child Adolesc Ment Health* [Internet]. 2018 Nov [cited 2023 Jan 19];23(4):303–12. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/camh.12252>

13. Cohodes EM, Kribakaran S, Odriozola P, Bakirci S, McCauley S, Hodges HR, et al. Migration related trauma and mental health among migrant children emigrating from Mexico and Central America to the United States: Effects on developmental neurobiology and implications for policy. *Dev Psychobiol* [Internet]. 2021 Sep [cited 2023 Jan 19];63(6). Available from: <https://onlinelibrary.wiley.com/doi/10.1002/dev.22158>
14. Scharpf F, Kaltenbach E, Nickerson A, Hecker T. A systematic review of socio-ecological factors contributing to risk and protection of the mental health of refugee children and adolescents. *Clin Psychol Rev* [Internet]. 2021 Feb [cited 2023 Jan 19];83:101930. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0272735820301185>
15. Rask S, Elo IT, Koskinen S, Lilja E, Koponen P, Castaneda AE. The association between discrimination and health: findings on Russian, Somali and Kurdish origin populations in Finland. *Eur J Public Health* [Internet]. 2018 Oct 1 [cited 2023 Jun 28];28(5):898–903. Available from: <https://academic.oup.com/eurpub/article/28/5/898/5033985>
16. Verelst A, Spaas C, Pfeiffer E, Devlieger I, Kankaapä R, Peltonen K, et al. Social Determinants of the Mental Health of Young Migrants. *Eur J Health Psychol* [Internet]. 2022 Jan [cited 2023 Aug 14];29(1):61–73. Available from: <https://econtent.hogrefe.com/doi/10.1027/2512-8442/a000097>
17. Staer T, Bjørknes R. Ethnic disproportionality in the child welfare system: A Norwegian national cohort study. *Child Youth Serv Rev* [Internet]. 2015 Sep [cited 2023 Jun 28];56:26–32. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0190740915001917>
18. Karlsson H. Is discrimination a driving force behind the over-representation of children with an immigrant background in Swedish out-of-home care? A quantitative study from Stockholm City. *Eur J Soc Work* [Internet]. 2021 Jul 4 [cited 2023 Aug 22];24(4):629–41. Available from: <https://www.tandfonline.com/doi/full/10.1080/13691457.2020.1793113>
19. Karlsson H. Is there an additional effect on the risk of entry into out-of-home care from having parent(s) born outside of Europe in cases of alleged physical child abuse? – findings from Sweden. *Nord Soc Work Res* [Internet]. 2022 Oct 2 [cited 2023 Aug 22];12(4):523–35. Available from: <https://www.tandfonline.com/doi/full/10.1080/2156857X.2020.1819392>
20. Vinnerljung B, Franzén E, Gustafsson B, Johansson I. Out-of-home care among immigrant children in Sweden: a national cohort study. *Int J Soc Welf* [Internet]. 2008 Oct [cited 2023 Aug 22];17(4):301–11. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1468-2397.2008.00568.x>
21. Obućina O, Ilmakunnas I. Poverty and Overcrowding among Immigrant Children in an Emerging Destination: Evidence from Finland. *Child Indic Res* [Internet]. 2020 Dec 1;13(6):2031–53. Available from: <https://doi.org/10.1007/s12187-020-09743-7>
22. *Coming of Age in Exile - Health and socio-economic inequalities in young refugees in the Nordic welfare societies.* København: Københavns Universitet; 2020 p. 127.
23. Matikka, Anni, Wikström, Katja, Halme, Nina. *Maahanmuuttajataustaisten nuorten hyvinvointi ja sen seuranta* [Internet]. 2015. (Tutkimuksesta tiiviisti). Available from: <https://urn.fi/URN:ISBN:978-952-302-522-6>
24. Timshel I, Montgomery E, Dalgaard NT. A systematic review of risk and protective factors associated with family related violence in refugee families. *Child Abuse Negl* [Internet]. 2017 Aug [cited 2023 Aug 14];70:315–30. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S014521341730251X>
25. Fisher C. Changed and Changing Gender and Family Roles and Domestic Violence in African Refugee Background Communities Post-Settlement in Perth, Australia. *Violence Women* [Internet]. 2013 Jul [cited 2023 Sep 5];19(7):833–47. Available from: <http://journals.sagepub.com/doi/10.1177/1077801213497535>

26. Bryant RA, Edwards B, Creamer M, O'Donnell M, Forbes D, Felmingham KL, et al. The effect of post-traumatic stress disorder on refugees' parenting and their children's mental health: a cohort study. *Lancet Public Health* [Internet]. 2018 May [cited 2023 Aug 17];3(5):e249–58. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2468266718300513>
27. Montgomery E. Refugee children's mental health and development - A public health problem in Europe. *Torture J* [Internet]. 2022 Jun 13 [cited 2023 Aug 14];32(1–2):163–71. Available from: <https://tidsskrift.dk/torture-journal/article/view/131756>
28. Rutanen N, Vehkalahti K. Lasten ja nuorten tutkimuseetiikan muuttuvat kentät. In 2019. p. 7–31.
29. Bronstein I, Montgomery P, Dobrowolski S. PTSD in asylum-seeking male adolescents from Afghanistan. *J Trauma Stress*. 2012;25(5):551–7.
30. Leavey G, King M, Barnes J, Hollins K, Papadopoulos C, Grayson K. Psychological disorder amongst refugee and migrant schoolchildren in London. *Soc Psychiatry Psychiatr Epidemiol* [Internet]. 2004 Mar 1 [cited 2023 May 9];39(3):191–5. Available from: <http://link.springer.com/10.1007/s00127-004-0724-x>
31. Dettlaff AJ, Cardoso JB. Mental health need and service use among Latino children of immigrants in the child welfare system. *Child Youth Serv Rev* [Internet]. 2010;32(10):1373–9. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2010-17145-013&site=ehost-liveORCID:0000-0002-4042-7282jberger@mail.utexas.edualand@uic.edu>
32. Gao X, Zhao Y, Wang N, Yang L. Migration modulates the prevalence of ASD and ADHD: a systematic review and meta-analysis. *BMC Psychiatry* [Internet]. 2022 Dec [cited 2023 May 9];22(1):395. Available from: <https://bmcp psychiatry.biomedcentral.com/articles/10.1186/s12888-022-04037-4>
33. Seeman MV. Similar psychosis risks in adoptees and immigrants. *Int J Soc Psychiatry*. 2020;66(3):292–9.
34. Abraham ZK, Sher L. Adolescent suicide as a global public health issue. *Int J Adolesc Med Health* [Internet]. 2019;31(4):1–9. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2019-56920-002&site=ehost-livezebib.abraham@mountsinai.org>
35. Luster T, Qin D, Bates L, Rana M, Lee JA. Successful adaptation among Sudanese unaccompanied minors: Perspectives of youth and foster parents. *Child Glob J Child Res* [Internet]. 2010;17(2):197–211. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2010-16531-004&site=ehost-livebateslau@msu.edu>
36. Finno-Velasquez M, Cardoso JB, Dettlaff AJ, Hurlburt MS. Effects of parent immigration status on mental health service use among Latino children referred to child welfare. *Psychiatr Serv* [Internet]. 2016;67(2):192–8. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2016-21328-007&site=ehost-livefinno@usc.edu>
37. Thomas S, Nafees B, Bhugra D. 'I was running away from death' - the pre-flight experiences of unaccompanied asylum seeking children in the UK. *Child Care Health Dev* [Internet]. 2004;30(2):113–22. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2004-11061-003&site=ehost-liveSamThomas1973@aol.com>
38. Murray JS. Toxic stress and child refugees. *J Spec Pediatr Nurs* [Internet]. 2018;23(1):1–5. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2018-00368-002&site=ehost-liveORCID:0000-0002-7397-8718JMurray325@aol.com>

39. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health* [Internet]. 2017 Aug [cited 2023 Jun 21];2(8):e356–66. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2468266717301184>
40. Geltman PL, Grant-Knight W, Ellis H, Landgraf JM. The “lost boys” of Sudan: use of health services and functional health outcomes of unaccompanied refugee minors resettled in the U.S. *J Immigr Minor Health*. 2008;10(5):389–96.
41. Grumi S, Milani L, Di Blasio P. Risk assessment in a multicultural context: Risk and protective factors in the decision to place children in foster care. *Child Youth Serv Rev* [Internet]. 2017;77:69–75. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2017-22138-010&site=ehost-liveORCID: 0000-0003-0218-458XORCID: 0000-0003-4353-3803serena.grumi@unicatt.it>
42. Rajendran K, Chemtob CM. Factors associated with service use among immigrants in the child welfare system. *Eval Program Plann* [Internet]. 2010;33(3):317–23. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2010-06917-016&site=ehost-liveClaude.chemtob@mssm.eduKushmand.rajendran@mssm.edu>
43. Pedrini L, Sisti D, Tiberti A, Preti A, Fabiani M, Ferraresi L, et al. Reasons and pathways of first-time consultations at child and adolescent mental health services: an observational study in Italy. *Child Adolesc Psychiatry Ment Health* [Internet]. 2015 Dec [cited 2023 Jan 19];9(1):29. Available from: <https://capmh.biomedcentral.com/articles/10.1186/s13034-015-0060-9>
44. Scribner R. Editorial: Paradox as Paradigm-The Health Outcomes of Mexican Americans. *Am J Public Health*. 1996;86(2):303–4.
45. Alegria M, Álvarez K, DiMarzio K. Immigration and Mental Health. *Curr Epidemiol Rep* [Internet]. 2017 Jun [cited 2023 Jan 19];4(2):145–55. Available from: <http://link.springer.com/10.1007/s40471-017-0111-2>
46. Chun H, Mobley M. The “Immigrant Paradox” Phenomenon: Assessing Problem Behaviors and Risk Factors Among Immigrant and Native Adolescents. *J Prim Prev* [Internet]. 2014 Oct [cited 2023 Jun 21];35(5):339–56. Available from: <http://link.springer.com/10.1007/s10935-014-0359-y>
47. Chang CD. Social Determinants of Health and Health Disparities Among Immigrants and their Children. *Curr Probl Pediatr Adolesc Health Care* [Internet]. 2019 Jan [cited 2023 Jun 20];49(1):23–30. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1538544218301755>
48. Seeman MV. Similar psychosis risks in adoptees and immigrants. *Int J Soc Psychiatry* [Internet]. 2020 May [cited 2023 Jan 19];66(3):292–9. Available from: <http://journals.sagepub.com/doi/10.1177/0020764020903324>
49. Kirkbride JB. Addressing ethnic inequalities in the pathways to care for psychosis. *BMC Med* [Internet]. 2018 Dec [cited 2023 Aug 18];16(1):240. Available from: <https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-018-1236-y>
50. Kirkbride JB, Errazuriz A, Croudace TJ, Morgan C, Jackson D, Boydell J, et al. Incidence of Schizophrenia and Other Psychoses in England, 1950–2009: A Systematic Review and Meta-Analyses. Scott JG, editor. *PLoS ONE* [Internet]. 2012 Mar 22 [cited 2023 Aug 19];7(3):e31660. Available from: <https://dx.plos.org/10.1371/journal.pone.0031660>
51. Hjern A, Palacios J, Vinnerljung B. Early childhood adversity and non-affective psychosis: a study of refugees and international adoptees in Sweden. *Psychol Med* [Internet]. 2023 Apr [cited 2023 Aug 14];53(5):1914–23. Available from: https://www.cambridge.org/core/product/identifier/S003329172100355X/type/journal_article

52. Brandt L, Henssler J, Müller M, Wall S, Gabel D, Heinz A. Risk of Psychosis Among Refugees: A Systematic Review and Meta-analysis. *JAMA Psychiatry* [Internet]. 2019 Nov 1 [cited 2023 Aug 19];76(11):1133. Available from: <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2747572>
53. El Bouhaddani S, Van Domburgh L, Schaefer B, Doreleijers TAH, Veling W. Psychotic experiences among ethnic majority and minority adolescents and the role of discrimination and ethnic identity. *Soc Psychiatry Psychiatr Epidemiol* [Internet]. 2019 Mar [cited 2023 Aug 20];54(3):343–53. Available from: <http://link.springer.com/10.1007/s00127-019-01658-1>
54. Bradby H, Varyani M, Oglethorpe R, Raine W, White I, Helen M. British Asian families and the use of child and adolescent mental health services: A qualitative study of a hard to reach group. *Soc Sci Med* [Internet]. 2007 Dec [cited 2023 Jan 19];65(12):2413–24. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0277953607004054>
55. Handulle A, Vassenden A. ‘The art of kindergarten drop off’: how young Norwegian-Somali parents perform ethnicity to avoid reports to Child Welfare Services. *Eur J Soc Work* [Internet]. 2021 May 4 [cited 2023 Aug 23];24(3):469–80. Available from: <https://www.tandfonline.com/doi/full/10.1080/13691457.2020.1713053>
56. Nordberg C. Invisibilised Visions: Migrant mothers and the reordering of citizenship in a Nordic welfare state context. *Nord J Migr Res* [Internet]. 2015 Jun 1 [cited 2023 Aug 23];5(2):67. Available from: <https://journal-njmr.org/article/10.1515/njmr-2015-0011/>
57. Blignault I, Saab H, Woodland L, Giourgas K, Baddah H. Promoting Mental Health and Wellbeing in Multicultural Australia: A Collaborative Regional Approach. *Int J Environ Res Public Health* [Internet]. 2022 Feb 26 [cited 2023 Jan 19];19(5):2723. Available from: <https://www.mdpi.com/1660-4601/19/5/2723>
58. Kim G, Aguado Loi CX, Chiriboga DA, Jang Y, Parmelee P, Allen RS. Limited English proficiency as a barrier to mental health service use: A study of Latino and Asian immigrants with psychiatric disorders. *J Psychiatr Res* [Internet]. 2011 Jan [cited 2023 Jan 19];45(1):104–10. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S002239561000141X>
59. Wohler Y, Dantas JA. Barriers Accessing Mental Health Services Among Culturally and Linguistically Diverse (CALD) Immigrant Women in Australia: Policy Implications. *J Immigr Minor Health* [Internet]. 2017 Jun [cited 2023 Jan 19];19(3):697–701. Available from: <http://link.springer.com/10.1007/s10903-016-0402-6>
60. Castaneda, Anu E.; Rask, Shadia; Koponen, Päivikki; Mölsä, Mulki; Koskinen, Seppo. Maahanmuuttajien terveys ja hyvinvointi - Tutkimus venäläis-, somalialais- ja kurditaustaisista Suomessa [Internet]. 2012. Available from: <http://www.julkari.fi/handle/10024/90907>
61. Hiitola J. Family life in transition : borders, transnational mobility, and welfare society in Nordic countries. Abingdon Oxon ; Routledge; 2020. (Routledge studies in family sociology).
62. Sirriyeh A, Ní Raghallaigh M. Foster care, recognition and transitions to adulthood for unaccompanied asylum seeking young people in England and Ireland. *Child Youth Serv Rev* [Internet]. 2018;92:89–97. Available from: <https://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2018-10550-001&site=ehost-liveala.sirriyeh@liverpool.ac.uk>



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INCLUSIVE APPROACH OUTCOMES IN DEVELOPMENT PROJECTS FOR CULTURAL AND LINGUISTIC MINORITIES – AN INTERVIEW STUDY

ABSTRACT

A Finnish initiative called TUULI project, led by the Finnish Institute for Health and Welfare, was launched in 2019 to respond to the need of providing accessible psychoeducational material for newly arrived refugees and for professionals working with them. This study investigates the co-creation process of the TUULI project and how participants of refugee backgrounds and professionals working with them perceived said process. Furthermore, this study investigates the factors that need to be considered to enable meaningful participation and to ensure experience of inclusion for cultural and linguistic minorities. The data were collected by semi-structured, in-depth interviews from 10 participants, five of whom were experts working with refugees and five of whom were of refugee backgrounds, using Teams video software. The interviews were recorded with consent and professionally transcribed for analysis. The data were analysed with thematic analysis, which included familiarization, coding, grouping, sorting, reviewing and revising, and, lastly, formulating the main themes and subthemes. The key themes pertaining to factors that need to be considered were centred on personal factors, cultural factors, factors related to the community and societal factors. The importance of providing feedback throughout the project, iterative communication with the participants, involving the target group at every stage of the project and the facilitation of a supportive and safe environment were emphasized. Participants had mostly positive perceptions of the co-creation process; they felt heard, included and safe enough to share their opinions and express their views. According to their viewpoints, the project was executed, managed and planned in a satisfactory manner, leading to gains on both personal and professional levels. Issues and challenges related to the project included communication breakdowns, prolonged duration, technical issues when conducting the remotely held meetings, and the feeling of insufficient inclusion of the target group in shaping the agenda and content of the project. The findings highlight the importance of a thorough and multifaceted approach in development projects involving cultural and linguistic minorities. This includes active engagement of the community under investigation, fostering effective and continuous interactive communication as well as ensuring the provision of feedback to participants during and after a project.

KEYWORDS: MENTAL HEALTH, REFUGEES, CO-CREATION, PARTICIPATORY METHODS, SERVICE DESIGN, DOUBLE DIAMOND, PSYCHOEDUCATION

INTRODUCTION

There are millions of forcibly displaced people worldwide, including 27.1 million refugees, who are particularly vulnerable to mental health issues [1,2]. Despite the evidently higher need for mental health services, people with refugee backgrounds often underutilize them due to self-stigma and other barriers such as public stigma, language barriers and lack of awareness or trust [3,4,5,6,7]. Refugees face various stressors throughout their migration process, which can lead to prolonged depression and anxiety [1,8].

In Finland, there is a mismatch between the need for mental healthcare services and their utilization amongst refugees [9]. People with refugee backgrounds have poorer overall health and receive lower-intensity care compared to native Finns [10,11]. There is no one-size-fits-all solution to address the mental health needs of refugees due to their diverse backgrounds and cultures [12]. According to Tuomisto et al. [13], the Finnish system for supporting the mental health of refugees is outdated and does not align with the current need due to an increase in the number of refugees and asylum seekers in Finland.

The Finnish Institute for Health and Welfare (THL) introduced the TUULI project for promoting the mental health of newly arrived refugees [14]. The goal of the TUULI project was to produce accessible and effective video-based psychoeducational material for newly arrived refugees and for professionals working with them – a need revealed by an earlier project, PALOMA [15]. The TUULI project was executed using the method of co-creation, comprising four stages according to the Double Diamond model [16] to investigate the perceived needs, circumstances and challenges related to mental health amongst refugees.

The Double Diamond model consists of four phases: discovery, definition, development and delivery [16]. In the TUULI project, the first phase included a survey to map out the current situation: 21 key informant interviews, three focus group interviews including peers and five focus group and three individual interviews with newly arrived refugees. The second phase included an all-day co-creation workshop run by service designers along with the TUULI project staff. The third phase included separate Teams workshops called ‘ideation afternoons’, which had 8 to 11 participants in each group. Ideation afternoons were a type of think tank where participants brainstormed together about the specifications of the videos. Altogether, 67 people participated in the co-creation workshop day and in the ideation afternoons. In the fourth phase, the project staff members compiled

the main message of each video along with focal points, forming a ‘script sketch’ that was based on the recordings of the workshops and the affinity diagrams made during the second phase.

The objective of the TUULI project was to produce easily accessible, high-quality and culturally sensitive video-based psychoeducation material that responds to the actual needs of newly arrived refugees. One purpose of the psychoeducational videos is to demonstrate that despite all the challenges related to mental health and integration there are people who were able to overcome those difficulties. The aim of these positive examples and stories is to reduce the stigma related to mental health issues and to promote help-seeking through social learning. The videos made for the TUULI project comprised 161 video clips, the total length being 1105 minutes. Twenty videos and three short documentaries were then constructed from those clips, with seven different languages to choose from, consisting of information, tips and stories about mental health, welfare and integration in Finland. The videos can be found on THL’s web page [14].

Altogether 114 healthcare professionals and individuals with refugee backgrounds participated in the co-creation process. 31 people with refugee backgrounds participated in the video recordings, and 137 quota refugees all over Finland were involved in the piloting of the videos. The scripts for the videos were all co-created, the information provided in the videos was written verbatim and the interview questions, themes and content were decided together with the participants of the co-creation process. The feedback obtained from the piloting was positive and resulted in no editing of the videos. It is reasonable to conclude that this is predominantly a result of the co-creation method.

Participatory methods have long been utilized as a component of research and development (RD) projects within THL, yet the absence of a comprehensive scientific assessment of their efficacy in the Finnish context points to a knowledge gap. In the TUULI project, the utilization of participatory methods enabled people to participate in the development of matters concerning themselves, thus contributing to the appropriateness and practicality of the services being developed. It is worth considering that the co-creation process of the TUULI project was mainly executed remotely due to the COVID-19 pandemic. As to the pandemic, new operating and remote methods have been brought to development work. The project was executed mainly online, and in addition to Zoom and Teams discussions, collaborative whiteboard platforms, heat maps

and voting were used to ensure participation in different ways.

This study investigates the co-creation process of the TUULI project and how participants of refugee backgrounds (i.e., the target group) and professionals working with them perceived said process. This study aims to fill the void mentioned in the previous paragraph, providing the much-needed empirical evidence on the effectiveness of participatory methods in Finland.

Furthermore, this study aims at determining what factors need to be considered to enable meaningful participation and to ensure experience of inclusion, especially for cultural and linguistic minorities (CLMs), from the viewpoints of the target group and the experts working with that group.

METHODS

STUDY POPULATION

A total of 10 individuals were interviewed via Teams video software, five of whom were experts working with refugees and five of whom were of refugee backgrounds. All 10 individuals had participated in the initial TUULI project. One member of the latter group was a social and healthcare professional working within the area of refugees' mental health. All the experts were familiar with issues around refugee mental health through their work, three of the experts were of the age group 50+ years, and two were aged between 30 and 49 years. Of the representatives of the target group (i.e., individuals with refugee backgrounds), three were aged between 30 and 49, one was 50+ years, and one was between 18 and 29 years of age. Of that same group, everyone's initial way of arriving in Finland was within the refugee quota, which means they have not spent time in a reception centre but were considered to be most in need of a resettlement by UNHCR. Time of residing in Finland ranged from 6 to 30 years. All interviews were conducted in Finnish. To safeguard the privacy of study participants and prevent readers from identifying them, no additional information about their demographics or specific field or title of work will be disclosed in this paper due to the limited size of the sample and the limited number of people working within this field in Finland.

In this study, a purposive sampling technique was employed by targeting and interviewing individuals who participated in the TUULI project. The selection of participants was based on their initial involvement in the project, ensuring their relevance to the research objectives. This approach allowed gathering of insights from key

stakeholders directly involved in the project. Due to outdated or lacking contact information, it was not possible to reach some of the participants of the TUULI project. 12 interview requests were sent, no reply was received for two.

DATA COLLECTION

A qualitative approach was used to gather information-rich data from the perspectives of both the target group and the experts working with them. This design enabled exploration of the participants' perceptions, understanding, experience and interpretation of the subject. The data were collected by semi-structured, in-depth interviews carried out remotely from October 2022 to December 2022, ranging in length from 45 to 90 minutes. The interviews were audio recorded with participants' consent and transcribed professionally for analysis. The transcripts underwent a thorough accuracy check and were anonymized by the interviewer, with any personal or community names removed, and all potentially identifiable information anonymized during the analysis to protect participant anonymity. Interviews covered three distinct themes, including 'co-creation and the meaning of participation', 'good practices of co-creation' and 'evaluation of the produced materials in the context of co-creation and participation'.

The interviews for this study were conducted in Finnish, since sufficient English skills could not be guaranteed from all the participants and therefore, there would have been a greater risk for misunderstandings or information breakdowns in the data. Conducting the interviews in Finnish and the analysis in English can potentially introduce risks and challenges for the process. To mitigate the risk of misinterpretation or bias, the interviewer implemented a strategy of recapping during the interviews. After the interviewee shared their perspective, the interviewer would summarize their understanding and ask for confirmation. This allowed validation of the interviewer's interpretation and ensured a more objective analysis. The interviewer and the person responsible for the analysis were the same, which promoted in-depth understanding, since they possessed first-hand knowledge and understanding of the interview context, nuances, and any clarifications sought during the interviews. This deep understanding contributes to a more accurate analysis and interpretation of the data. Since all of the interviewees were not native Finnish speakers, the interviewer used clear and simple language and explained the concepts used in the interview. The thematic frameworks for the interviews were carefully written and revised to avoid using complex terminology or

unclear questions. It was also made clear that anytime during the interview, the interviewee could ask clarifying questions or ask for a clearer definition of a concept.

DATA ANALYSIS

The data were analysed with thematic analysis. Firstly, the author familiarized themselves with the data by carefully reading through the data multiple times. Next, initial coding was done by coding segments of the data that were relevant to particular themes. Then, these segments were arranged on a document. After that, grouping was done by arranging all the segments to identify potential themes. Subsequently, trends and patterns in the data were recognized from the segments, and various codes were investigated to determine how they could be combined, and subthemes within the themes were identified. The themes were reviewed and revised to ensure that each of them had enough data to support it and that each theme was distinct from the others. Similar themes were merged together. Finally, the themes were formulated into a narrative conveying the overall message that emerged from the data. Overall, completing the thematic analysis involved several important steps, including familiarization, coding, grouping, sorting, reviewing and revising, and formulating themes. By following this process, emerging themes were identified and analysed, leading to a deeper understanding of the topic.

Table 1. What factors need to be considered to enable meaningful participation and to ensure experience of inclusion, especially for cultural and linguistic minorities: The main themes and subthemes

Main Theme	Subtheme
Creating Inclusive Spaces for Meaningful Participation	Valuing Contributions and Empowering Participation
	Creating a Safe Space to Share
	Feeling Heard and Understood
	Finding the Right Way and Time to Approach
Ethical and Cultural Considerations in Research and Development with Minority Populations	Individuality over Generalization
	Lost in Translation
	Family Matters
	Conducting Respectful and Beneficial Research and Development
Community-Centred Development: Listening, Learning and Responding	Needs-based and Feasible Interventions
	Participatory Planning and Inclusive Management
	Transparent Communication and Follow-Up
	Building a Bridge Between Communities
Creating Equitable and Inclusive Opportunities for Participation	Enabling Genuine Opportunity for Participation
	Ensuring Accessibility and Inclusivity
	Involving Participants at Every Stage
Foundations for Successful Integration: Education, Empowerment and Inclusion	Basic Education and Accessible Information
	Considering Diversity in Integration Processes

RESULTS

*FACTORS NEEDED TO BE CONSIDERED TO ENABLE MEANINGFUL PARTICIPATION AND TO ENSURE EXPERIENCE OF INCLUSION, ESPECIALLY FOR CULTURAL AND LINGUISTIC MINORITIES**Main theme 1: “Creating Inclusive Spaces for Meaningful Participation”*

This main theme embodies the thought that to enable meaningful participation and ensure a positive experience of inclusion for CLMs, it is necessary to create spaces that are safe, respectful, and responsive to participants’ needs and perspectives. This includes providing opportunities for active engagement, listening and valuing participants’ contributions, and using culturally appropriate approaches to communication and decision-making.

“Valuing Contributions and Empowering Participation” relates to the importance of participants feeling that their contributions are valued and have an impact. Participants in CLMs may often feel marginalized or excluded from decision-making processes, and it is important to create an environment where they feel empowered to share their thoughts and ideas.

“The experience of inclusion comes from the feeling that you can be involved in influencing a service or something similar, and from seeing that your opinion is important, it matters and there is a purpose behind the things that are done.” – Expert 5

“The experience of inclusion comes from making a person realize that they are involved, that they are genuinely wanted and that they are part of the development, and not just a number.” – Target group 4

“Creating a Safe Place to Share” pertains to the need for a safe and welcoming space for participants to share their experiences and perspectives. Participants may have experienced discrimination or marginalization in the past, and it is important to create a supportive environment where they feel comfortable and accepted. This subtheme initiated the importance of creating trust, genuine encounter as well as safe place and time.

“A safe space to discuss is important, instead of putting yourself up for evaluation, you get the feeling that this is a common issue, to which everyone brings their own perspectives.” – Expert 4

“Feeling Heard and Understood” relates to the importance of active listening and understanding. Participants want to feel that their voices are being heard and that their experiences are being understood. This requires creating an environment where participants feel comfortable expressing themselves and where there is an open dialogue between participants and researchers or developers. This subtheme acknowledges a respectful and appreciative atmosphere that is also open for criticism.

“There might not always be a solution, but the fact that a person feels heard and seen is already a lot.” – Expert 3

“Finding the Right Way and Time to Approach” pertains to the importance of a respectful and sensitive approach when working with CLMs. There is a need to be aware of the potential power dynamics at play and be mindful of the language, tone and approach when working with vulnerable groups. This requires building trust with participants and establishing a rapport based on mutual respect and understanding. This subtheme mentions respecting and acknowledging different backgrounds and the importance of being supportive.

“In Finland, we perhaps have this way of approaching quite directly and rapidly to the topic itself and we are able to speak about many different things, however, in some countries and cultures the appropriate approach might not be so direct.” – Expert 3

Main theme 2: “Ethical and Cultural Considerations in Research and Development with Minority Populations”

This main theme encompasses the idea that RD within CLMs requires careful and sensitive scrutinization of ethical issues and cultural differences that consider the unique needs, perspectives and experiences of the population under study and ensure respectful and responsible engagement with participants. It also recognizes the responsibility of conducting ethical RD that avoids harm, respects cultural norms, and involves community members in the development process.

“Individuality over Generalization” highlights the need for recognizing and respecting the diversity within CLMs. It emphasizes that individuals within these groups may have different beliefs, practices and experiences, and should thus be encountered above all as individuals instead of representatives of their culture or minority. Researchers and developers must take this into account in the planning and implementation of RD projects, and also keep in mind that success stories do not apply to everyone, however, they can motivate.

“A single person cannot represent the whole culture and on the other hand, if the person does not identify with that culture or religion, it might be that they say something they think others want to hear.” – Expert 5

“Lost in Translation” refers to the challenges of communicating effectively with CLMs, especially when language and cultural differences create barriers to understanding. It underscores the importance of using culturally appropriate communication strategies and considering alternative ways of conveying information. This subtheme recognizes the need to acknowledge and address differences in cultural beliefs, values and practices that may impact participation and communication. Culture itself rarely causes issues, the issues relate mostly to traumas, prejudice and misconceptions.

“Cultural differences must be taken into account: The word ‘research’ may evoke association with diseases and medicines in many people’s minds, many do not necessarily know that research is done for different things and for different purposes. Many people do not understand the aim of research and may also be afraid of opening up and the possible consequences.” – Target group 4

“Family Matters” recognizes the importance of family relationships and networks in many cultural and linguistic minority communities. It emphasizes the need for researchers and developers to understand and respect these dynamics, and to consider involving family members in the process when appropriate. This subtheme highlights the importance of recognizing and respecting the influence of family and community on individual decision-making and participation, even if it differs from the developer’s personal perception of the subject’s rights.

“It is not necessarily culturally sensitive that the client is alone at the reception and relatives are not allowed to enter the room. It may also be genuine care and the idea that the matter is shared. It may also be that the customer does not dare to talk about some things without the presence of a safe individual.” – Expert 5

“Conducting Respectful and Beneficial Research and Development” focuses on the ethical responsibilities of researchers or developers working with CLMs. It highlights the importance of respecting cultural norms, avoiding harm, maintaining confidentiality, and involving community members in the process in ways that are respectful and appropriate. The subtheme emphasizes the ethical responsibilities to ensure that RD is conducted in a way that minimizes harm and maximizes benefit for participants, that respects their rights, dignity and privacy. This subtheme also underlines the importance of not using someone’s past traumas as a means to promote researchers’ own agenda and ensuring that the participants receive something in return as well.

“It is important not to use the participant’s experience or wound to promote a cause, but to make sure that they get the feeling that they also get something from this, that they are listened and understood, and that their experience is taken into account.” – Target group 1

Main theme 3: “Community-centred Development: Listening, Learning and Responding”

This main theme encompasses the idea that development projects and successful solutions for addressing the needs of CLMs require careful planning, collaboration and feedback from the community. It emphasizes the importance of engaging with communities in a meaningful way to understand their needs, strengths and challenges, and to work collaboratively with them to develop viable solutions that are tailored to their context and culture.

“Needs-based and Feasible Interventions” highlights the importance of starting with a clear understanding of the community’s needs and priorities and ensuring that the development project is realistic and feasible. This involves identifying the root causes of issues related to mental health needs or barriers for help-seeking, and developing targeted interventions that address them.

“In order for people to genuinely develop things concerning themselves, there must be the acknowledgement that something needs improvement.”

– Target group 5

“Participatory Planning and Inclusive Management” emphasizes the need for a participatory and inclusive approach to project planning and management. This involves listening to the community’s thoughts and opinions and involving them in decision-making processes to ensure that the project and methods are well reasoned and effective, and not using a top-down approach to management. Careful consideration is required of who should be involved in the project and how they can be reached, and the use of methods that promote goal attainment.

“Working methods contribute to the purpose and it is justified why things are done in a certain way.”

– Expert 1

“Transparent Communication and Follow-up” highlights the importance of transparency and accountability in RD projects. This involves keeping participants informed about the purpose and progress of the project and providing them with feedback as well as the results in a transparent and accessible manner. Follow-up is also important to ensure that the project has achieved its goals and in evaluating its impact on the community.

“When developing things together, it is important to consider the participants’ motivation for participating and to make it clear what is being done. Motivation can decrease if the purpose and the entire process remain too obscure.” – Target group 1

“Building a Bridge between Communities” emphasizes the need to understand and appreciate the culture and context of the target community. This involves going beyond theoretical information and engaging with the community at their level to build trust and understanding. It also involves narrowing the gap between cultures to facilitate communication and collaboration, and to ensure that the project is culturally appropriate and relevant to the community.

“When linguistic and cultural minorities are involved in co-creation it is important for professionals working with these groups to have extensive knowledge of the

target group’s culture, background and how it is best to work with them, which issues belong to culture and which issues to religion.” – Target group 2

Main theme 4: “Creating Equitable and Inclusive Opportunities for Participation”

This main theme encompasses the idea that in order to enable meaningful participation and ensure a positive experience of inclusion for CLMs in service design, it is necessary to create equitable, genuine and inclusive structures and processes that support and enable participation for everyone at every step of the RD process.

“Enabling Genuine Opportunity for Participation” highlights the importance of creating structures and processes that enable individuals to participate in service development in a meaningful way. This includes providing adequate resources and accessibility accommodations to ensure that all individuals are given the opportunity to participate, as well as ensuring that participants understand the purpose and scope of the project.

“In order for people to be genuinely involved in developing things that concern themselves, one should in good faith give the possibility for development to take place and give people the opportunity to develop” – Expert 4

“Ensuring Accessibility and Inclusivity” emphasizes the need to ensure that participation is accessible to individuals from diverse backgrounds, including CLMs. This may involve providing language translation and interpretation services, as well as creating accessible and culturally appropriate materials and communication strategies.

“It would also be important that the methods and tools used were accessible to everyone, different opportunities and methods for participation would be offered in many ways, for example those struggling with technology would be offered some other form of participation, for example a call or a telephone interview.” – Expert 2

“Involving Participants at Every Stage” underscores the importance of involving participants at every stage of the service development process, from design and planning to implementation and dissemination, in order to ensure that their voices are heard, perspectives are valued and

those have a real impact. This includes soliciting feedback and incorporating participant experiences and perspectives into decision-making processes, as well as ensuring that participants are informed and engaged throughout the development process.

“The target group must be involved from the beginning in a sufficiently representative way already in the planning phase to enrich the groundwork. It is not enough to ask the target group to join in the next steps when the project is already underway. At that stage it would be difficult to understand the big picture and know what the project is about, how it started and how it has been developed and what is expected of them.” – Target group 4

Main theme 5: “Foundations for Successful Integration: Education, Empowerment and Inclusion”

This main theme encompasses the idea that minorities' inclusion into the society needs to begin already at the start of the integration process: successful integration of refugees, and other marginalized groups, requires a strong groundwork of basic understanding, empowerment and inclusion from the very beginning of the migration process. If this process does not succeed, it is not likely that representatives of CLMs would be willing or prepared to participate in developing services concerning themselves later on. This main theme introduces participation in a broader context, implying that experience of inclusion and meaningful participation is associated with successful integration. Together, these subthemes suggest that successful integration requires a proactive and holistic approach that lays the foundation for long-term social, economic and cultural integration. Overall, the main theme of “Foundations for Successful Integration” highlights the importance of providing a strong constitution for cultural and linguistic minorities to build upon in order to successfully integrate into the new society.

“Basic Education and Accessible Information” highlights the importance of providing basic education and information in a simple and accessible way, particularly for those who may be unfamiliar with societal norms and practices. This includes providing practical information about how things work in the society, as well as explaining basic concepts in a way that is easily understandable.

“Information about very practical things must be given.” – Target group 2

“Considering Diversity in Integration Processes” emphasizes the importance of considering the needs and perspectives of CLMs from the very beginning of their integration process. This includes taking a broad view of their skills and abilities, as well as addressing potential mental health issues. It also involves creating opportunities for them to feel included and have a voice in matters that concern them.

“Many people have skills, knowledge and experiences that would be useful for society, but in this country, they are ignored.” – Target group 3

“Everything should really begin from the moment a person enters to Finland; some kind of process would start, through which a person would get information and become a participant and member of the integration process.” – Target group 2

PARTICIPANTS' PERCEPTIONS OF THE CO-CREATION PROCESS OF THE TUULI PROJECT

Table 2. How did participants perceive the co-creation process of the TUULI project: The main themes and subthemes

Main Theme	Subtheme
Effective Participation and Inclusive Dialogue in Development Project	Empowering Participants to Feel Heard and Included
	Facilitating Inclusive and Supportive Discussions
	Facilitating a Safe and Trusting Space for Participants to Share
	The Value of Dynamics and Stimulating Conversations
Personal Growth and Positive Experiences in Participation	Personal Development and Professional Growth
	Empowering Participants to Feel Heard and Included
	Positive Experiences of Co-Creation
	The Mutual Benefits of Participant Involvement: Diversity of Expertise and Perspectives
Collaborative Project Management: Achieving Positive Outcomes through Effective Planning, Execution and Co-Creation	Effective Practices and Tools
	Positive Experiences with Video Recording and Interviews
	Effective Use of Participatory Methods and Techniques
	Broad Expertise
	Impactful Co-creation
Addressing Challenges in Development Project for Inclusive Participation and Successful Outcomes	Barriers to Inclusion: Technical and Logistical Challenges
	Lack of Information and Follow-up
	Insufficient Inclusion of Target Group's Voice
	Improvement Suggestions and Feedback
	Need For a Broader Reach
The Importance of My Participation	
The Impact of My Participation	

Main theme 1: “Effective Participation and Inclusive Dialogue in Development Project”

This main theme focuses on the importance of effective communication and inclusive dialogue in the TUULI project, and supports the idea that the project allowed effective communication and interaction between participants with diverse backgrounds and perspectives, as well as provided a supportive and safe space for sharing those said perspectives, and moreover, ensured that all participants felt heard and included. Overall, the importance of mutual respect, trust, and understanding between all stakeholders involved in the project was raised.

“Empowering Participants to Feel Heard and Included” is characterized by the participants’ feelings of being able to express themselves and contribute to the development process, as well as feeling that their opinions and experiences were valued and considered. Participants felt a sense of empowerment, which led to a positive experience of inclusion. This subtheme highlights the importance of creating an inclusive environment where participants feel comfortable sharing their thoughts and ideas without fear of judgement or exclusion. The subtheme emphasizes the significance of effective participation, active listening, facilitation and feedback in fostering an experience of inclusion and being heard.

“The experience of inclusion was enhanced by being listened to and having the opportunity to speak and bring up one’s own thoughts and opinions in the group.” – Target group 2

“I got the feeling that my work experience, opinions, views and thoughts had meaning and weighed in the development work” – Expert 3

“Facilitating Inclusive and Supportive Discussions” focuses on the importance of supportive and inclusive facilitation in creating an environment that promotes meaningful participation. This subtheme highlights the role of facilitators in creating an open and welcoming atmosphere where everyone’s opinions and experiences are valued, giving space and support to participants, and encouraging them to share their experiences and ideas in a non-judgemental manner. Participants appreciated the approach of the facilitators, who were present, encouraging and helpful, creating an inclusive and comfortable atmosphere. This subtheme also emphasizes the importance of facilitators

having been attentive and having ensured equal opportunities for all as well as fostering a sense of community and collaboration.

“The facilitators’ working method was participative, they were present and gave space” – Expert 1

“The facilitator’s clarifying questions and taking care of the working group’s atmosphere made it possible for all participants to be listened to.” – Expert 4

“Facilitating a Safe and Trusting Space for Participants to Share” highlights the importance of creating a respectful and safe environment for participants. Practices such as going through rules and establishing trust at the beginning, as well as discussing the concept of a safe space, were viewed positively. The extracts also suggest that the facilitators were invested in the topic and showed a genuine interest in supporting the participants.

The subtheme “The Value of Dynamics and Stimulating Conversations” focuses on the quality of communication and interaction during the co-creation process. Participants emphasized the importance of good and active discussion, effective sharing of knowledge and information, and meaningful group interactions. They appreciated the opportunity to engage in productive discussions and appreciated the process of narrowing down the most essential aspects. The workshops were praised for their enthusiastic and interactive atmosphere, with small group settings being particularly highlighted. The peer-to-peer learning and interaction was considered beneficial, and the dialogue was seen as a valuable aspect of the co-creation process. Overall, this subtheme highlights the importance of creating an open, safe and interactive environment that facilitates effective communication and meaningful interactions between participants.

Main theme 2: “Personal Growth and Positive Experiences in Participation”

This theme emphasizes the personal development and positive experiences that participants gained through their involvement in the TUULI project. It also highlights the personal benefits of participation, including the sense of meaning and importance that came from being involved in the project, as well as the opportunities for personal and professional growth that participation can provide.

“Personal Development and Professional Growth” relates to the personal and professional growth of the participants. The project provided them with new ideas, knowledge and perspectives that they could apply to their work and personal lives. The participants felt that the project was important not only for their professional identity but also for their personal growth. It gave them a sense of belonging and helped them overcome challenging life situations. The project also allowed them to distance themselves from their work and gain new insights, which added freshness to their work.

“The project significantly affected the experience of inclusion on a personal level: it opened up my own, personal knots, influenced my mood, helped me gain new perspectives. It also affected my family, friendships and work environment.” – Target group 1

“The project was important also from the point of view of my own professional identity and attitude.” – Expert 4

“The project gave me new ideas and information for my own work.” – Expert 1

“Empowering Participants to Feel Heard and Included” highlights the participants’ positive experience of feeling valued, important and heard during their involvement in the project. They expressed that their participation was not only interesting and important, but it also gave them a sense of being part of a community and that their contribution had an impact on the result. The participants felt appreciated, and their expertise and personal experiences were acknowledged and valued. Additionally, some participants felt that their participation allowed them to provide unique perspectives that other experts may not have been able to share. Overall, this subtheme emphasizes the importance of creating an inclusive and supportive environment that values and recognizes the contributions of all participants.

“My participation in the videos was important, as an expert-by-experience I was able to share information about how people feel and what could help in the best way - information that experts may not be able to convey.” – Target group 5

“Positive Experiences of Co-creation” reflects the participants’ positive experiences and feelings towards their

participation in the project. Participants expressed their satisfaction with the end result and the overall project. They also mentioned that they had a common goal and felt motivated and enthusiastic about their involvement. The subtheme includes expressions of happiness, contentment and a sense of accomplishment. The participants also appreciated the opportunity to be part of a community and work with a diverse group of people. The subtheme highlights the importance of a positive atmosphere and a sense of togetherness in the co-creation project.

“The atmosphere was nice and encouraging, the whole project was functional and unhurried, and the multi-professional activity exuded” – Expert 3

“The participation left a positive feeling, impact and mood. I am very happy that I could be a part of this project and that I could share my own thoughts and try to promote them.” – Target group 2

“The Mutual Benefits of Participant Involvement: Diversity of Expertise and Perspectives” highlights the diverse range of expertise and perspectives brought by the participants, including experience working with refugees, knowledge of mental health challenges and insights from different professional backgrounds. The project gained valuable knowledge and insights from participants’ experiences, which were essential for developing practical solutions. Participants’ unique perspectives and expertise were considered helpful in expanding the scope of the project and generating innovative solutions.

“From my participation, the project gained realistic information about the mental health situation of refugees and which factors influence on the background from both aspects: through my work and my own user experience, i.e., a broad perspective on the subject.” – Target group 2

Main theme 3: “Collaborative Project Management: Achieving Positive Outcomes through Effective Planning, Execution and Co-creation”

This main theme can be described as the overarching idea that emerged from the perceptions of positive co-creation in the TUULI project. Overall, this main theme emphasizes the importance of effective planning, execution and co-creation in collaborative project management, and highlights the

specific practices, tools and techniques that can be used to achieve positive outcomes.

“Effective Practices and Tools” highlights various practices and tools that have proven to be effective in the implementation of the project. The subtheme captures the essence of the data extracts, which emphasize the importance of tools and practices such as multilingual materials, clear communication, expert groups and technology that have been instrumental in ensuring the project’s success. The subtheme demonstrates the significance of effective practices and tools in fostering collaboration, communication and participation amongst the project’s stakeholders, which all were essential in achieving the project’s objectives.

“Good practice was a well-thought-out and illustrative process diagram and description of what will happen next and how long it will take.” – Expert 4

“Positive Experiences with Video Recording and Interviews” describes the positive experiences and benefits of the video recording and interview process in the project. The participants mention how the process allowed them to express their thoughts and feelings freely and in detail without a script, and how the interviews with the psychologist were particularly engaging. They also appreciated the pleasant demeanour of the filming crew and interviewer, and how the process was stress-free and did not require any prior practice. Additionally, some participants found the time and effort invested in travelling to Helsinki for the interviews and video recording to be worth it.

“The shooting of the videos was a situation, which enabled talking about different things and feelings in detail, freely and exhaustively without a script.” – Target group 4

“Effective Use of Participatory Methods and Techniques” underscores the importance of using effective participatory methods and techniques to ensure that all voices are heard and that everyone is engaged in the process. The extracts mention the use of multilingual materials, clear questions, visible notes, and the use of techniques like voting and process diagrams as well as the importance of having experts and representatives from target groups involved in the process. The subtheme highlights the success of participatory techniques and methods in ensuring that everyone is engaged and feels heard.

“In the TUULI project, the voting was especially participative: it was the first time that voting was done in a situation that involved experts, it was truly a great combination. It was both engaging and eye-opening.” – Expert 5

“Broad Expertise” revolves around the importance and benefits of having diverse and comprehensive participation in a project or initiative and highlights the presence and contribution of participants from different backgrounds, professions and expertise, including representatives of the target group and professionals working with them. The use of good practices such as involving key stakeholders and partner organizations in the project’s decision-making process were also mentioned.

“A good practice was that the partners, for example the Ministry of Health and Social Affairs, the Immigration Office, different municipalities, the traumatology centre, the employment office, all such partners that work with the target group were involved in the steering group or otherwise cooperated with the project” – Target group 2

“Impactful Co-creation” highlights the importance of collaboration in the development of videos related to mental health and migration. The use of collaborative approaches expanded the content and topics covered in the videos and helped identify the appropriate level of text and content. The collaborative approach also generated a wealth of information and insights into the target audience, which helped inform the development of video content. The use of collaborative approaches also ensured that the videos were easily approachable and understandable, and the resulting videos were varied, comprehensive and accessible. The collaborative approach also brought to light insights that may not have been discovered otherwise, and the involvement of a wide range of experts helped inform the development of video content.

Main theme 4: “Addressing Challenges in Development Project for Inclusive Participation and Successful Outcomes”

This theme focuses on the various challenges encountered in the co-creation project, including technical and logistical issues, communication breakdowns and insufficient inclusion of the target group’s voice. The subthemes suggest that the participants had varying perceptions of their level of

engagement and participation in the project, with some feeling that they had limited influence in shaping the agenda and content of the project. The subthemes highlight the need for a more comprehensive approach to project development that includes a broader range of topics and participants, effective communication and follow-up, as the interviewees expressed their desire for more information and updates after the project ended as well as receiving regular feedback to drive improvement.

“Barriers to Inclusion: Technical and logistical challenges” describes various challenges related to the technical and logistical aspects of the project, such as difficulties with web tools, scheduling and language barriers. Some participants felt that being present would have been more productive or enjoyable, while others felt that technical challenges detracted from their sense of participation. Additionally, there were concerns about limits being placed on what could be discussed during certain stages of the project. Despite these challenges, participants worked together to find solutions, such as providing extra time for someone with limited language skills to express themselves or finding ways to manage technical issues as they arose.

“Lack of Information and Follow-up” highlights the importance of effective communication and follow-up after the project was completed. Participants expressed the need for regular updates on the progress of the project, clear information on the project’s outcomes and a feedback mechanism for them to share their opinions and concerns. They also suggested that a more interactive process could have been implemented, such as regular feedback sessions. Participants felt that better communication and follow-up would have increased their sense of ownership and engagement in the project and would have helped to ensure that the project’s outcomes were sustained over time.

“It was unclear how certain choices were arrived at, for example in terms of language or substance, those reasons could have been brought out more through, for example, interim reports.” – Expert 4

“I would have hoped for a more interactive process and information about what things have been dealt with, where we currently are at and where we are going. Some kind of feedback discussion after the project would have been good. There was uncertainty about whether the project affected services, in which way THL employees benefitted from the project, and how the materials are used.” – Target group 1

“Insufficient Inclusion of Target Group’s Voice” discusses the importance of involving and engaging the target group in the project to increase their sense of participation and ownership. Participants expressed their desire for more opportunities to shape the project’s direction and agenda, and for more space and speaking time during project activities. They also suggest that having more representatives from the target group in project leadership and planning could help ensure that the project better reflects their needs and priorities. Finally, participants expressed disappointment that they did not feel that they had much influence over the project or opportunities to contribute to its development.

“Development work was done together in a good and positive way, but the positioning was however such that most of the ideas and materials had already been thought through and the impact of the target group was small.” – Target group 4

“I got the feeling that the agenda was ready, and we were there just to relate.” – Target group 1

“Improvement Suggestions and Feedback” introduces participants’ suggestions for changes or improvements that could have been made to enhance the project’s outcomes. Some feedback suggested that the project could have been more efficient. Additionally, feedback about the use of videos and tools suggests that not everyone was on the same page, implying the need for better communication and training. Suggestion to allocate speaking turns instead of having free discussions was also raised.

“Need for a Broader Reach” shares a common theme of suggesting that the project could have been more inclusive, targeted a broader audience and included a wider topic selection. Participants felt that certain topics and groups were left out of the discussion, and that the project would have benefitted from including more diverse perspectives. This subtheme captures the idea of inclusivity and expanding the scope of the project to encompass a wider range of issues and individuals.

“The audience and target group could also have been broader, aimed more at the whole society.” – Target group 1

“The search for interviewees could have been done more widely, the elderly were not included at all, the senior citizens were forgotten.” – Target group 2

The last two themes are individual themes that conclude the main message of the participants.

“The Importance of My Participation” focuses on the participants’ experience of inclusion and their perception of how much their participation meant for the project. Overall, participants felt that their participation in the project was meaningful, nobody felt their participation did not matter at all. All the participants concurred that the project was important and necessary, some who only took part in one phase of the project felt that their participation amongst the large group did not have great significance.

“The Impact of My Participation” explores participants’ thoughts about the effectiveness of their participation and the impact it had on the project’s outcome. Individual contributions and perspectives are mentioned as participants describe how they brought their unique experiences, insights and perspectives to the project, and how these contributed to the final videos. Additionally, the effect on target audience and society is also present, as participants describe the impact that the videos had on the target audience, how they challenged preconceptions and opened new perspectives. Finally, personal growth and empowerment emerges, as participants discuss how their involvement in the project has affected their own lives and sense of agency, as well as how it has given them a platform to speak out on important issues.

“In the videos, I see points of view that I brought up and that I myself have influenced. I brought the points of view of families with children, pregnant women, family-centredness, especially the point of view of those in a vulnerable position, such as asylum seekers and the undocumented and furthermore, the impact of parenting on the child’s growth and development.”
– Expert 3

“Videos change opinions, at the first video you may be surprised, but when you watch the following videos, your mind changes. Videos affect people’s minds, I found. Talking directly about one’s own depression and weaknesses had that effect, in many cultures or even in Finland it is not customary for a man to talk so directly about his weaknesses. When my family and friends saw the videos, they realized that I am not the only person who has had difficulties. They noticed that you have to respect the fact that there are many types of people in the world.” – Target group 3

DISCUSSION

Successful development project implementation within CLMs is strongly linked to provision of continuous feedback throughout the project, iterative communication with the participants, inclusive involvement of the target group at every stage and fostering a safe and supportive environment. Despite the challenges observed, such as communication issues and feelings of insufficient inclusion, the participants reported a positive experience and a sense of personal and professional growth. The findings are in line with previous research on the subject. For example, considering the role and participation of family members was brought up in both previous research [3,17] and the findings of this study. Similarly, being able to relate to the research staff, benefit from the project somehow and help the community by creating feasible solutions that lead to an actual change in the society were brought up as enabling and motivating factors for participation in both previous research [18] and the findings of this study. In the review by George et al. [18], the importance of making participation convenient by arranging childcare or transport services as well as designing the study setting as safe, comfortable and non-invasive as possible was mentioned as an enabling factor. Similar thoughts were shared by van den Muijsenbergh et al. [19], with the addition that including researchers with similar backgrounds would be valuable to enhance participants’ cultural congruence.

Participants felt that the atmosphere of the TUULI project was safe, encouraging and empowering. They felt comfortable to share their experiences without fear of being judged or excluded. What is described here is a concept of ‘psychological safety’, which is “a shared belief amongst team members that it is safe to take interpersonal risks” [20]. In their 2016 article, Roussin et al. state that this concept relates to participants feeling comfortable to speak up, share their opinions and present suggestions without fearing negative feedback or other negative consequences. This creates an environment that supports and facilitates learning, creativity and innovation, whereas the absence of psychological safety might result in withholding of ideas, especially negative comments or suggestions for improvement, potentially leading to a lack of dedication by the participants.

In the interviews, many participants said they would have wished for more inclusion of the target group also in the steering group and moreover, being involved in shaping the agenda of the project. This theme of involving the target group more profoundly and at every stage was discussed

considerably in many interviews, especially in those with representatives of the target group. These notions along with previous knowledge on the subject serve as a significant takeaway and are of utmost importance to be improved in future endeavours when developing services or support measures especially for minority populations.

A few interviewees mentioned the wish for discussing and dealing with more painful issues in terms of topic choices for the videos, such as talking about suicide, honour violence and the rights of sexual minorities. While these are important topics to touch on, the purpose of the TUULI project was to make the videos easily approachable, encouraging and suitable for anyone to watch. The TUULI project, directed towards refugees arriving in the country, was consciously designed to maintain a hopeful and motivating atmosphere in the videos, acknowledging the potential fragile state of mind of these individuals. Newly arrived refugees are most likely dealing with a lot of emotions and stressors at that stage of the migration process, and adding to that load can potentially be too shocking and something they are not ready to deal with at that stage. Furthermore, the topics and themes of the videos were voted on in the third phase of the TUULI project, and the topics discussed in the videos were democratically selected amongst the proposed ones. If all the proposed topics had been discussed in the videos, the scope of the TUULI project would have been expanded excessively, and the designated timeline would probably have been exceeded as well.

The interviews also brought up minor criticisms and uncertainty as to whether the process was truly equal, as many felt that they were there only to share their experiences and were not able to greatly influence the project's agenda or its planning. One of the reasons for this feeling could be the fact that three of the people with a refugee background participated only in the last phase. However, this same topic also emerged in the literature as a criticism of the use of participatory methods in RD projects [21,22], and should therefore be scrutinized when planning to use participatory methods amongst these groups. Similarly, Ross et al. [23] raised that same notion about the community's involvement in all areas of a development project, including leadership, decision-making and implementation. In their 2010 article, the authors highlight the active involvement of the community at all stages of a project, starting from interactive planning of the project and its methods, all the way to dissemination and use of findings. As stated previously, this theme emerged in many of the interviews.

There were no major discrepancies between the experts

and the representatives of the target group in how the project was perceived and graded overall. The participants who only took part in two or less phases felt they had less ability to influence, whereas the ones who were involved in three or more felt they were able to have an impact on the content of the videos. Overall, when asked to estimate the impact and importance of participating in the project, nobody felt that their participation had little or no importance or impact. The experts had more similarity in the answers compared to the representatives of the target group, amongst whom there was more dispersion in the answers to both estimates.

There were participants representing the target group at every stage of the TUULI project, but as for people who participated in the previous stages, a significant amount of data was not obtained due to outdated or missing contact information, also the two requests that were not replied to were sent to representatives of the target group who participated in the first two phases of the TUULI project. The larger number of those who participated in the last stage could partly be explained by the fact that they might have been more equipped to participate in the interview, because they had also participated in the filming stage and were perhaps braver and more prepared to speak than others. In the future, it would be useful to involve a consistent group of individuals, known as a 'core group', throughout all the stages of a project. This would ensure that reliable data is acquired while also making the participants feel that their participation has a tangible impact on the planning and execution of the project.

Psychoeducation and videos were integral components of the initial project plan, which necessitated a more concrete approach during the funding application process, and for that reason, participatory methods were not used when defining the needs of the project. Certain aspects had to be well defined in advance, as they played a crucial role in determining the feasibility and potential impact of the project. Thus, flexibility was limited in order to meet the requirements of the funding application and ensure a comprehensive understanding of the proposed initiative. However, based on previous projects and research, and according to the World Health Organization, psychoeducation is a recommended form of psychosocial support for refugees [24,25].

When implementing co-creation, it is important to consider its limitations and potential disadvantages. While co-creation is a valuable tool for uncovering insights and perspectives that may not occur to experts or researchers due to the practical nature of the subject, and for breaking down the hierarchy between decision-makers and stakeholders,

it is essential to recognize that certain voices may not be heard. There can be various reasons why someone may be unwilling or unable to articulate their opinion [26]. Emphasizing individuality over generalization, and being mindful over whose voice is represented and whose is not, was also brought up in many interviews, both within experts and within representatives of the target group. That indicates that co-creation requires time, thorough reflection and profound effort from start to finish, while continuously minding research ethics. Power relations between developers/researchers and the target population as well as within the community under scrutiny need to be considered at every stage. Power relations are a complex web and if not reflected in the beginning of a project, it might not result in positive societal changes. Furthermore, there is always the risk that vulnerable communities are included in the decision-making only seemingly, but power relations are neglected or not considered extensively, i.e., organizations promote their version of participation solely from the perspective that something can be said to have been developed in collaboration with the stakeholders [27].

In general, co-creation has the potential to bring together different actors, like academics, experts and civil society members, who are all driven by different incentives, objectives and roles and can learn from each other. Dialogue is the key for a successful collaboration, and the communication between different actors should be comprehensive and open, and participants should be committed to the cause [28]. Facilitators act as knowledge brokers and intermediaries. They play a crucial role in the co-creation process guiding group discussions, ensuring active participation and creating a fair and trusting environment. The facilitator inspires the participants by posing questions and adding different perspectives, keeping the focus on the joint outcome rather than individual agendas [29]. In the interviews conducted for this study, the role of the facilitators was brought up on several occasions: participants appreciated facilitators who were seen as encouraging and helpful, having ensured equal opportunities for everyone to speak freely and creating a safe and respectful environment to share even the most sensitive matters. The role of knowledge brokers and intermediaries can be valuable in various fields, including psychiatry.

Stier & Smit [28] conclude that successful co-creation is more than just the combined knowledge or understanding of the participants. People's collective acquisition of knowledge, the exchange of ideas through individual learning, and their interactive experiences serve to augment the overall comprehension and generate novel insights around the

subject. In the co-creation process, synergy and new perspectives emerge, thus exceeding the initial understanding of the individual participants. In this way, the whole can be larger and more versatile than originally expected. In psychiatry, collaboration and co-creation can be beneficial in developing interventions, treatment plans and policies that address mental health challenges. The involvement of multiple stakeholders, including researchers, clinicians, patients, families and organizations can lead to more comprehensive and effective approaches to mental healthcare.

Co-creation can be used in several ways in the care of mental health problems. The TUULI project and this study have shown that, when developing psychoeducation or other interventions, it is of great significance to include the individuals that the interventions are being developed for. Moreover, participating in a co-creation process can also have an empowering and stigma-reducing effect on the target group themselves, and also professionals can gain new knowledge through the process. When developing interventions, co-creation can enhance the collaboration between researchers, clinicians and patients to develop new interventions, therapies and treatment models. By engaging all relevant stakeholders, including individuals with lived experience of mental health conditions, co-creation ensures that interventions are based on real-world needs, are culturally sensitive and address the diverse experiences of patients. In a broader sense, co-creation promotes collaboration, inclusivity and patient-centred approaches, which recognise the importance of diverse perspectives and shared decision-making.

Some suggestions for future research could be: 1. Examining the factors that contribute to the creation of safe and respectful environments for participation in development projects for CLMs, and how these environments can be fostered and sustained over time, 2. Investigating the long-term impact of participation in development projects on participants and their communities, including the potential for personal and community-level growth and development, 3. Exploring the potential for digital and online platforms and interventions to support mental health of refugees, and the unique challenges and opportunities associated with these platforms and 4. Investigating the effectiveness of mental health interventions tailored to refugees' cultural backgrounds and experiences integrated into existing refugee resettlement programmes.

The mental health of people with refugee backgrounds is a wide topic as is the use of participatory methods in development projects. Therefore, these suggestions are just a

few potential study topics, and there are many other avenues to explore in this area of research.

CONCLUSIONS

This study reports a wide range of prerequisites and factors that need to be taken into consideration to enable participation and to ensure experience of inclusion for CLMs. These entail: personal factors, including the need for spaces that are safe, respectful and responsive to participants' needs and perspectives; cultural factors, including careful consideration of ethical issues and cultural differences as well as underlining individuality; factors related to the community, including listening to the community's needs, responding to those needs as well as creating genuine opportunities for the community to be involved at every stage of the project, and societal factors, including a society free from discrimination, investing in education, empowerment and inclusion of minorities. Many of these factors relate to the researchers', developers' or project managers' responsibility to conduct ethical, respectful and responsible RD and their role in facilitating inclusive atmosphere and communication, including the importance of giving feedback throughout the project and after it.

The findings indicate the need for thorough and multifaceted consideration when conducting RD amongst CLMs to enable true and genuine participation for these groups, and an inclusive and asset-based integration process, which identifies and leverages the strengths and abilities of individuals to support their successful integration into society that begins when a person relocates into the country. Overall, the findings also indicate the need to address socio-cultural aspects to gain a better understanding and recognition of the influence of these aspects on CLMs' health and wellbeing, and providing culturally safe and effective services for these groups.

Participants of the TUULI project had various perceptions concerning the co-creation process of the project, mostly on the positive side. Participants felt heard, included and safe enough to share their opinions and mostly had the experience of a well-executed, well-managed and well-planned project that used participatory methods in engaging stakeholders on a wide spectrum. Participants gained from the project on a personal and professional level and felt that the atmosphere supported growth on both levels and perceived mutual benefits of the co-creation process. However, some challenges were also faced, including technical

issues, communication breakdowns, prolonged duration and the feeling of insufficient inclusion of the target group in shaping the agenda and content of the project. A critique raised by all the participants was a lack of informing and feedback during and after the project. Some participants also brought up their wish for a broader reach and an expansion of the target group and the subjects of the videos. In conclusion, enabling true and genuine participation includes active engagement of the community under investigation, fostering effective and continuous, interactive communication, whilst not forgetting to provide feedback to participants during and after a project.

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References

1. The World Health Organization. Mental health and forced displacement. Published 2021. Accessed [2022 June 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/mental-health-and-forced-displacement>.
2. United Nations High Commissioner for Refugees (UNHCR). Global Trends Report 2021. Published June 2022. Accessed [2022 June 13]. Available from: <https://www.unhcr.org/62a9d1494/global-trends-report-2021>.
3. Giacco D, Laxhamp N, Priebe S. Prevalence of and risk factors for mental disorders in refugees. *Semin Cell Dev Biol*. 2018;77:144-152. doi: 10.1016/j.semcdb.2017.11.030.
4. Byrow Y, Pajak R, McMahon T, Rajouria A, Nickerson A. Barriers to Mental Health Help-Seeking amongst Refugee Men. *Int J Environ Res Public Health*. 2019;16(15):2634. doi: 10.3390/ijerph16152634.
5. Noubani A, Diaconu K, Ghandour L, El Koussa M, Loffreda G, Saleh S. A community-based system dynamics approach for understanding factors affecting mental Health and Health seeking behaviors in Beirut and Beqaa regions of Lebanon. *Global Health*. 2020;16(1):28. doi: 10.1186/s12992-020-00556-5.
6. Harris SM, Sandal GM, Bye HH, Palinkas LA, Binder PE. Integration Is Correlated with Mental Health Help-Seeking From the General Practitioner: Syrian Refugees' Preferences and Perceived Barriers. *Front Public Health*. 2021;9:777582. doi: 10.3389/fpubh
7. Ahmadinia H, Eriksson-Backa K, Nikou S. Health-seeking behaviours of immigrants, asylum seekers and refugees in Europe: a systematic review of peer-reviewed articles. *J Doc*. 2021;ahead-of-print. doi: 10.1108/JD-10-2020-0168.
8. Schick M, Zumwald A, Knöpfli B, et al. Challenging future, challenging past: the relationship of social integration and psychological impairment in traumatized refugees. *Eur J Psychotraumatol*. 2016;7:28057. doi: 10.3402/ejpt.v7.28057.
9. Castaneda A, Cilenti K, Mäki-Opas J, Abdulhamed R, Garoff F. Psykkinen hyvinvointi. In: Kuusio H, Seppänen A, Jokela S, Somersalo L, Lilja E, editors. *Ulkomaalaistaustaisten terveys ja hyvinvointi. FinMonik-tutkimus 2018-2019*. Publications of Finnish Institute of Health and Welfare, Report; 2020.
10. Skogberg N, Mustonen K, Koponen P, et al. Turvapaikanhakijoiden terveys ja hyvinvointi. Tutkimus Suomeen vuonna 2018 tulleista turvapaikanhakijoista. Finnish Institute for Health and Welfare. Report 12/2019, 412 pages. Helsinki.
11. Kiesepää V, Jokela M, Holm M, Suvisaari J, Gissler M, Lehti V. Posttraumatic stress disorder among immigrants living in Finland: Comorbidity and mental health service use. *Psychiatry Res*. 2021;300:113940. doi: 10.1016/j.psychres.2021.113940.
12. Leask CF, Sandlund M, Skelton DA, et al. Framework, principles and recommendations for utilising participatory methodologies in the co-creation and evaluation of public health interventions. *Res Involv Engagem*. 2019;5:2. doi: 10.1186/s40900-018-0136-9.
13. Tuomisto K, Tiittala P, Keskimäki I, Helve O. Refugee crisis in Finland: Challenges to safeguarding the right to health for asylum seekers. *Health Policy*. 2019;123(9):825-832.
14. Finnish Institute for Health and Welfare. Mental Health for Migration: Psychoeducation and Mental Health Promotion for Newly Arrived Refugees (TUULI). Published June 13, 2022. Accessed [2022 Dec 16]. Available from: <https://thl.fi/en/web/thlfi-en/research-and-development/research-and-projects/mental-health-for-migration-psychoeducation-and-mental-health-promotion-for-newly-arrived-refugees-tuuli>.

15. Finnish Institute for Health and Welfare. The PALOMA project – Improving mental health services for refugees. Published Apr 19, 2021. Accessed [2022 Dec 16]. <https://thl.fi/en/web/thlfi-en/research-and-development/research-and-projects/the-paloma-project-improving-mental-health-services-for-refugees>.
16. Design Council. Framework for Innovation: Design Council’s evolved Double Diamond. Published May 19, 2019. Accessed [2022 Dec 16]. Available from: <https://www.designcouncil.org.uk/our-work/skills-learning/tools-frameworks/framework-for-innovation-design-councils-evolved-double-diamond/>
17. Cooper S, Enticott JC, Shawyer F, Meadows G. Determinants of Mental Illness amongst Humanitarian Migrants: Longitudinal Analysis of Findings From the First Three Waves of a Large Cohort Study. *Front Psychiatry*. 2019;10:545. doi: 10.3389/fpsyt.2019.00545.
18. George S, Duran N, Norris K. A Systematic Review of Barriers and Facilitators to Minority Research Participation amongst African Americans, Latinos, Asian Americans, and Pacific Islanders. *Am J Public Health*. 2014;104(2):e16–e31. doi: 10.2105/AJPH.2013.301706.
19. van den Muijsenbergh M, Teunissen E, van Weel-Baumgarten E, van Weel C. Giving voice to the voiceless: how to involve vulnerable migrants in healthcare research. *Br J Gen Pract*. 2016 Jun;66(647):284–5.
20. Roussin CJ, MacLean TL, Rudolph JW. The Safety in Unsafe Teams: A Multilevel Approach to Team Psychological Safety. *J Manag*. 2016;42(6):1409–1433. doi: 10.1177/0149206314525204.
21. Aldridge J. Working with vulnerable groups in social research: Dilemmas by default and design. *Qual Res*. 2014;14(1):112–130. doi: 10.1177/1468794112455041.
22. Ozkul D. Participatory Research: Still a One-Sided Research Agenda? *Migrat Lett*. 2020 Apr 2;17(2):229–37.
23. Ross LF, Loup A, Nelson RM, et al. Human Subjects Protections in Community-Engaged Research: A Research Ethics Framework. *J Empir Res Hum Res Ethics*. 2010;5(1):5–17. doi: 10.1525/jer.2010.5.1.5.
24. Giacco D, Matanov A, Priebe S. Providing mental healthcare to immigrants: current challenges and new strategies. *Curr Opin Psychiatry*. 2014 Jul;27(4):282–8.
25. World Health Organization. Mental Health and Psychosocial Support for Refugees, Asylum Seekers and Migrants on the Move in Europe: A multi-agency guidance note. Published Dec 14, 2015. Accessed [2023 Jul 3]
26. Leino H, Puumala E. What can co-creation do for the citizens? Applying co-creation for the promotion of participation in cities. *Environ Plann C*. 2021;39(4):781–799.
27. Rose D. Participatory research: real or imagined. *Soc Psychiatry Psychiatr Epidemiol*. 2018;53:765–771. doi: 10.1007/s00127-018-1549-3.
28. Stier J, Smit SE. Co-creation as an innovative setting to improve the uptake of scientific knowledge: overcoming obstacles, understanding considerations and applying enablers to improve scientific impact in society. *Journal of Innovation and Entrepreneurship*. 2021 Sep 26;10(1):35.
29. Bornbaum CC, Kornas K, Peirson L, Rosella LC. Exploring the function and effectiveness of knowledge brokers as facilitators of knowledge translation in health-related settings: A systematic review and thematic analysis. *Implementation Science*. 2015;10:162-174.



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EQUINE-FACILITATED THERAPY IN TREATING AN ASYLUM SEEKER GIRL WITH POST-TRAUMATIC STRESS DISORDER: A CASE STUDY

ABSTRACT

Previous studies exist in using equine-facilitated therapy (EFT) in treating post-traumatic stress disorder (PTSD), however, no studies among refugees or asylum seekers were found. This study aimed at describing and analysing a 12-week EFT process for an asylum seeker girl with PTSD. The polyvagal theory was used as theoretical background, where strengthening the body-mind's system for regulating arousal is stressed. The case subject was a 13-year-old girl "Meryam", born in the Middle East, who had entered Finland eight months before the EFT process started. No interpreter was used in the process. The EFT sessions were videotaped and analysed. The methodological approach based on grounded theory. The analyses ended up forming three main categories of relevant contents involving: 1) anxiety regulation and growing the window of tolerance, 2) reciprocal expression of needs and desires and increasing of agency, and 3) strengthening the body-mind integration. All of these increased during the process, observed both in the sessions and in real life. The horse played a crucial role in the process: it acted as a force of attraction that motivated the patient to stretch her window of tolerance in order to be able to perform desired actions, such as riding. Both the therapist and the horse need to be competent in offering enough safety for the patient at all times in the therapeutic triangle. One advantage in using EFT with this target group was the small need for shared spoken language. This paper contends that EFT can be used with this target group.

KEYWORDS: ADOLESCENT, ANXIETY, ASYLUM SEEKER, CASE STUDY, EQUINE-ASSISTED THERAPY, EQUINE-FACILITATED THERAPY, HIPPO THERAPY, MIGRANT, POST-TRAUMATIC STRESS DISORDER (PTSD), REFUGEE

INTRODUCTION

FORCIBLY DISPLACED PEOPLE AND TRAUMATIZATION

The United Nations High Commissioner for Refugees (UNHCR) estimated that global displacement reached a record high at the end of the year 2018, with little hope of improvement in sight. Ongoing mass conflicts around the globe and the resulting flow of displaced people have increased clinical and academic interest in the practice of treating traumatized refugees in the Western world. Also, a debate is going on whether traumas should be treated already during the asylum phase, with the right to be treated on one hand and the worry of doing harm if the treatment is interrupted, for instance, in the case of negative asylum decision on the other hand.

In Finnish population-based migrant samples, the prevalence of having at least one potentially traumatic experience in the former home country (e.g., witnessing a violent death/injury or being a victim of a serious physical attack/harm) was as high as 77% among the Kurdish origin adults, and as many as 35% of the Kurdish men had experienced torture [1]. The psychiatric symptom levels have also been found to be high: whereas the prevalence of severe depressive and anxiety symptoms in the Finnish general population was 10%, among Kurdish origin adults in Finland, the respective figure was as much as 35%, and even 49% among the Kurdish women [2].

Refugee and asylum seeker children and adolescents have been studied somewhat less in Finland, but recent results among the newly arrived asylum seekers point out that as many as 87% of the 13–17-year-olds, 73% of the 7–12-year-olds and 54% of the 0–6-year-olds had experienced at least one potentially traumatic event before entering Finland [3]. Among the adolescents, 40% had witnessed physical violence towards another person, 25% had been harmed (or attempted) physically, 43% had lost a loved person and 21% had unwillingly been separated from their family. Furthermore, symptom levels were also found to be high: 35% of the adolescents had psychosocial symptoms, mainly problems in peer-relations (53%) or emotional symptoms (43%) [4].

Thus, the alarmingly high levels of potentially traumatic experiences and psychiatric symptoms call for attention in treating traumas, post-traumatic stress disorder (PTSD) and other psychiatric symptoms among refugees and asylum seekers, adults as well as children.

Equine-facilitated therapy (EFT) in treating post-traumatic stress disorder and traumas

Equine-facilitated therapy (EFT) is characterized by including a horse in a therapeutic triangle as another therapist in addition to the professional human therapist, who engages the horse in the therapeutic process to facilitate the desired changes, for instance, psychological and social insights in psychotherapeutic context. Thus, the therapeutic alliance between the patient, the therapist and the horse, and the attractive force of the horse are some of the key factors in EFT, in comparison to corresponding therapies without the horse. In Finland, EFT is always conducted by a health or social service professional (e.g., physiotherapist, occupational therapist, psychologist, psychotherapist, medical doctor or social worker) who has an additional 3-year EFT education.

The use of EFT in treating PTSD or traumatized patients has been still only scarcely studied and documented [5–6]. Some case studies and quantitative pilot studies with small samples have shown promising preliminary results among traumatized adults [7–8] and adolescents [9–13], although not involving control groups or randomization. These studies have stressed that the horse may have a unique potential to aid the desired psychological changes in traumatized patients in positive attachment, safety, emotion regulation, social skills and body awareness. Thus, EFT may be considered a promising treatment for traumatized patients, but needs more investigation, documentation and understanding.

EQUINE-FACILITATED THERAPY (EFT) IN TREATING REFUGEES AND ASYLUM SEEKERS

Studies in using EFT with refugee or asylum seeker patients were not found, either among adults, adolescents or children, or in treating PTSD or other domains. However, this target group might be of great interest in this field of research and clinical practice, for various reasons.

Firstly, EFT is a holistic approach involving the whole mind-body continuum that is usually emphasized when treating refugees with complex traumatization [14]. For instance, the rehabilitation centres for torture victims generally use multi-professional and holistic ways of treating traumas, usually including physiotherapy. Secondly, it has been discussed that more traditional psychotherapy, based mainly on Western concepts and stressing the role of speech and verbal reflection, might be a somewhat unfamiliar approach for non-Western people. Thus, traditions of psychotherapy involving more flexible, functional, non-verbal or creative methods have been suggested, such as using music,

other art or movement for working with non-Western people. Thirdly, language barriers have been sometimes named as a challenge in psychotherapeutic treatment of migrants, even via a professional interpreter, whereas in EFT, language does not play such a major role as in a more traditional psychotherapy setting. Therefore, it can be hypothesized that EFT may serve as a suitable approach when treating traumatized refugees.

THE POLYVAGAL THEORY AND TRAUMATIZATION

The polyvagal theory was introduced in the 1990s by Stephen Porges [15]. According to the theory, the autonomic nervous system can be divided into three distinct parts, hierarchical in relation with each other: 1) parasympathetic system's dorsal vagal complex or "vegetative vagus" where the most primal survival strategies and primitive autonomic control results in suppressing of vital functions (for instance, when animals freeze when threatened, conserving their metabolic resources); 2) sympathetic system which is the more evolved one and associated with the regulation of sympathetic fight or flight behaviours, and 3) parasympathetic system's ventral vagal complex or "smart vagus" which is the most evolved one in social involvement and can inhibit or disinhibit defensive limbic circuits, depending on the situation, in the service of social affiliative behaviours, such as communication and self-calming. Thus, the theory outlines the structure of two functionally distinct branches of the vagus nerve, both associated with a different adaptive behavioural strategy to a frightening situation and both inhibitory in nature via the parasympathetic nervous system in opposition to the sympathetic-adrenal system, which is involved in mobilization behaviours.

The polyvagal approach has been used in theorizing traumatization and in the development of trauma treatments and rehabilitation [16–17]. The theory stresses the importance to focus on strengthening the body-mind's system for regulating arousal when treating trauma, PTSD, anxiety and depressive symptoms caused by traumatization. Practical applications of the polyvagal theory have resulted in positive observations, especially in the treatment of emotional trauma.

AIMS OF THE STUDY

This study targeted describing and analysing a 12-session EFT process with a case of an adolescent asylum seeker girl with PTSD. With this detailed description and analysis,

the use of EFT with this target group may be evaluated, developed and enhanced.

METHODS

CASE SUBJECT

The case subject in this study was a 13-year-old girl called "Meryam", born in the Middle East. Meryam had entered the country of Finland as an asylum seeker eight months before the EFT process started. Meryam received a temporary residence permit in the beginning of the EFT process and a social security number with rights to use the services as a municipal citizen by the end of the process. Thus, during the EFT process Meryam was not yet entirely in general services and still partly in the asylum services. She started to go to school already during the asylum phase. She lived in Finland with her mother and siblings.

Based on the background information Meryam had been a victim of physical family violence, sexual violence and restraint during her childhood and adolescence. Meryam was diagnosed with PTSD and had received psychotherapy services during the asylum process. She had a lot of anxiety and fears that limited her daily functioning. She performed well in school and was obedient and well in contact, but was not able to go out alone, thus she stayed a lot at home and was not able to travel to school by herself. She had many somatic symptoms and pains in her body, e.g., stomach pain, joint ache and headaches. She was referred to the EFT process by the treating psychotherapist (A-C Q-O; later referred to as referring psychotherapist), thus serving partly as a parallel process with psychodynamic psychotherapy, although she did not receive other therapies during the EFT process. She had visited medical doctors several times during the asylum phase due to pains and injuries in different parts of the body.

Meryam had no significant prior experience with riding, but had expressed interest toward animals and especially horses. She spoke and understood only very little Finnish in the beginning of the EFT process.

EQUINE-FACILITATED THERAPY PROCESS

The 12-week process consisted of altogether 12 sessions, from 60 to 75 minutes each, that took place once a week from July to September 2019. Meryam cancelled two of the planned 12 EFT sessions due to somatic health reasons. One of the cancellations was replaced with an EFT session during the same week as the cancelled one and the other

was substituted with a session at home at the end of the process. Thus, the 12-week process included 11 EFT sessions and a final home visit.

The treating professional was an EFT student with an education and clinical experience of psychologist and psychotherapist (AEC; later referred to as therapist in the process). The horse in the process was a 15-year-old Icelandic mare, experienced in socio-pedagogical horse activity services but not in EFT per se. The stable where the process took place was a rather small stable in Southern Finland specialized in socio-pedagogical horse activities. In addition to Meryam, the horse and the therapist, the referring psychotherapist joined in seven of the 11 EFT sessions to film and to assist in creating an atmosphere of safety for Meryam (sessions I-II, IV-V, VII, IX-X). In the other four of the 11 EFT sessions, the referring psychotherapist was replaced by other stable personnel to film (sessions III, VI, VIII, XI). In addition, the clinical work supervisor, an experienced psychiatrist and EFT therapist (TM; later referred to as supervisor), joined in to observe two of the sessions (sessions III, VIII). The stable's other horses also took part in the sessions to a small extent. In the final session (XII), the therapist and the referring psychotherapist visited Meryam's home.

The EFT process was free of charge for Meryam due to the process being a part of the therapist's EFT education. No interpreter was used in any of the 12 sessions, but in the final home visit the parent acted as an interpreter to a small extent. The therapist transported Meryam by car, back and forth, to the stable to every session (45 minutes per direction), joined by the referring psychotherapist for seven of the 11 times. Thus, the car trips served as extra time to chat a little via Google Translator and to enjoy some snacks together.

DOCUMENTATION AND DATA ANALYSES

Prior to the beginning of the 12-week process the therapist together with the supervisor roughly sketched the EFT process goals, based on the approximate background information received of the case subject. In addition, prior to each of the 12 sessions, a plan was drafted by the therapist and revised by the supervisor that outlined the aims, contents and timetable of each individual session.

The 11 EFT sessions held in the stable were videotaped in entirety with a video camera. Within a couple of days after each session, the therapist watched and analysed the raw videotape (from 60 to 75 minutes), and edited a shorter version (from 20 to 25 minutes), that included the most important moments of that session. In addition, the

therapist wrote down a transcription of all observations and reflections made during every session while watching the videotape. The supervisor watched every edited video and commented on the transcription prior to the next session. The final home session was not recorded, but was planned and transcribed with the supervisor the same as the EFT sessions. In addition, the therapist wrote a clinical report of the process after the final session, revised by the supervisor, to be used in the clinical setting and planning of the service path for Meryam in the future.

In analysing the data, the methodological approach was based on grounded theory [18] where the raw data is coded and categorized by the themes that emerge in it. The raw videos were analysed and edited by selecting moments that pointed out relevant psychopathological perspectives and observations or changes in emotional, cognitive, behavioural or bodily levels of Meryam. These psychopathological perspectives could be observed either within Meryam or in her relationship with the horse, the therapist or other surroundings (as other people, other horses or the stable).

RESULTS

The 11 EFT sessions included, e.g., getting the horse from the pasture, brushing, nursing and tending the horse, walking and mastering the horse, riding in the paddock and in the stable's garden, braiding the horse's hair, feeding the horse and cleaning the stable. Riding the horse in the paddock included mostly gait and a small amount of tölt, leading the direction and the speed of the horse (e.g., stopping, turning, zigzagging cones) both with and without the therapist, stretching hands and body in different ways etc. The first nine EFT sessions started with going through the forthcoming session with picture cards.

The tentative aims for the EFT process were to strengthen the more traditional psychodynamic psychotherapy process by involving the body-mind-integration, to grow Meryam's self-confidence, courage, self-efficacy, and to reduce her anxiety. After the first sessions these became more accurate with growing anxiety regulation and self-efficacy, resulting in the ability to function better in everyday life (e.g., to go out alone). The sessions I-III aimed mainly at establishing the client-therapist-horse-contact and creating a clinical construction of the case, the sessions XI-XII at closing the 12-week process, and the sessions in between at working with Meryam's clinical issues. The more specific aims of the sessions IV-XI included: strengthening the feeling of

safety; growing courage, self-confidence, self-efficacy and expression; growing the window of tolerance of fear and anxiety; increasing the abilities of self-calming; living with the fearful memories and integrating them as a part of self and life history, thus making room for joy and peacefulness, and strengthening the body-mind integration and bodily control.

The analyses of the raw videotapes and the reflective transcriptions ended up forming three main categories of relevant contents involving: 1) fear and anxiety regulation and growing the window of tolerance; 2) reciprocal expression of needs and desires and increasing of agency, and 3) strengthening the body-mind integration. Each of them is described below in detail, although in reality operating in an interlinked fashion.

FEAR AND ANXIETY REGULATION AND GROWING THE WINDOW OF TOLERANCE

Anxiety regulation and working with the window of tolerance was the most noticeable theme throughout the whole EFT process. Meryam showed rather traditional symptoms of PTSD, such as getting frightened, startling and wincing easily, or crying out for fright. Anxiety was observed also with some displacement activity, such as whisking off flies when there weren't any and cleaning herself with nothing to clean. The startling symptom was seen throughout the process but whisking and cleaning reduced towards the end of the process.

From session I, Meryam's interest towards the horse was notable, with simultaneous strain. Thus, with the force of attraction the horse pulled Meryam to the limits of her anxiety tolerance, but letting Meryam decide the pace of going towards anxiety. This was seen, for instance, when riding the horse, it was simultaneously the most interesting and the most frightening thing for Meryam. In session II, Meryam showed a great deal of pride and joy when riding the horse for the first time, and in session III she stated the aspiration to ride, but when the moment of mounting the horse came, she pulled back due to the anxiety, and showed disappointment and sadness for not being able to perform the act she on the other hand desired. In session IV, the therapist decided that they do other things than ride, calmer things such as tending the horse and braiding its hair. In session V, Meryam got again the chance to decide to ride or not, and she decided to do so. She showed again clear joy and satisfaction with herself (e.g., smiling, laughing, making jokes) in being able to overcome her fears and handling the feelings of anxiety when wanting to achieve something that

was desired for her (to ride the horse). She warmly hugged and thanked the horse in Finnish language after dismounting, showing satisfaction, relief and appreciation.

Many more surprising real-time happenings in the stable also made it possible to study very concretely the theme of fear and anxiety regulation. For instance, in session IV, when taking the horses from the pasture, the horse surprisingly galloped near Meryam, frightening her greatly. The therapist helped Meryam to calm down: she was physically near to Meryam, and stayed calm, demonstrated bodily indications of fright (e.g., heart beating and trembling) and modelled "stopping" the situation and stabilizing herself by breathing and grounding. In session V, the therapist stopped in the same place where the fright had happened the last time to go through it in a peaceful manner and to model self-calming inner speech. Meryam stated the feeling of nervousness but showed with her thumb, a thumbs up, when ready to continue. When walking the horse from the pasture, Meryam got scared and anxious again from hearing the thrash of the horse's hooves from behind thus triggering a flashback from the last time. The therapist intercepted the situation and they explored together the feelings with calmness and continued to walk when Meryam felt calm enough. In sessions V and VI, Meryam decided to not let another horse walk behind her, thus not hearing the thrash of the hooves from her back, crossing the limits of her window of tolerance. With this experience, however, Meryam understood the idea of escaping the fears versus facing them, and onwards from session VII she decided, step by step, to start to walk with hearing the frightening thrash of the hooves from behind and desensitize herself. Thus, she understood the logic and started to intentionally widen her window of tolerance and to regulate the anxiety she felt when the flashbacks emerged, ending in session XI with walking and hearing the thrash of the hooves behind her, but without feeling anxious.

In the car after session VI, a conversation via Google Translator between Meryam, the therapist and the referring psychotherapist emerged regarding fearing memories and encountering fears. Meryam stated, for instance, that she tried to forget all the difficult memories from the former home country, but that it was impossible to be without them coming to mind time after time. She stated that when being in the stable and with the horse, she could forget the difficult memories for a second and live in the moment, whereas at home she was surrounded with the memories all the time. The theme of going towards the fears and conquering the fears instead of running from them was discussed, although the experiences in the former home country were not discussed.

Another example of anxiety regulation and growing the window of tolerance was seen when mounting the horse. In session V, when Meryam was anxious with mounting, she quickly “jumped” from the pedestal to the back of the horse. In session VI, the therapist instructed her to stop and breathe a couple of times during the mounting process, so that the calmness in action was achieved by stopping and breathing, and the process continued in a calm manner, although the action was frightening in the first place.

These concrete moments, experienced with the horse due to its pulling power and with the guidance of the therapist, made it possible for Meryam to stop and concretely feel the anxiety rising and declining, thus regulating the feeling instead of escaping it. During several moments throughout the process, the happenings with the horse and in the stables made it possible for Meryam and the therapist to demonstrate the beating of the heart and self-calming by stopping and breathing. The therapist was all the time available for Meryam to participate and help her in anxiety regulation. This warranted particular calmness and an extra relaxed atmosphere from the therapist. For instance, when the horse splashed and Meryam got frightened, she instantly looked to the therapist for her reaction and was able to continue when seeing the therapist modelling relaxation and calmness. In session VIII, in a moment while riding the horse in a calm, relaxed, joyful moment, the therapist instructed a short version of a “safe place exercise” so that it was possible for Meryam to also use that in her everyday life.

Since there was no shared spoken language between Meryam and the therapist, they used several symbols when communicating Meryam’s real-time anxiety levels. One of the ways of communication was using the thumbs: Meryam pointed out the level of anxiety with the thumbs up (no great anxiety), thumbs down (too much anxiety, need to wait before continuing) and thumb in the middle (somewhat tolerable level of anxiety, continuation but with care). Another way of communication was using a code language of colours for different emotions that were first shortly discussed with Meryam with pictures in the stable (red for anger or great trouble, yellow for milder distress or discomfort, blue for sadness, and green for joy and peacefulness). In addition to just communicative purposes, this of course taught Meryam also to separate and name different emotions, to notify when different emotions emerge in the self, to communicate the emotions to others and to manage them and regulate them. The pictures with different colours for different emotions included also pictures of some simple ways to encounter the

emotions, such as breathing, counting or helping oneself to pause.

RECIPROCAL EXPRESSION OF NEEDS AND DESIRES AND INCREASING OF AGENCY

Another theme that was strongly observed throughout the process was the reciprocal expression of needs and desires and increasing of agency of Meryam. Although without being particularly shy or timid, in session I, Meryam stated many times “it doesn’t matter” although there seemed discomfort towards her (e.g., wet shoes). However, already in session II and increasingly in forthcoming sessions she started to express herself to the therapist rather a lot: her interests, observations, wishes, discomforts, fears, likes and dislikes. She also, from the first sessions, started to be humorous and make jokes although playing with limited linguistic possibilities with expression.

In session VII, Meryam states, while riding, that she wants to try to trot with the horse. This was also a big gesture of growing agency, self-efficacy and expression. The therapist made a quick decision to let Meryam tölt three short distances to get the experience of general responsiveness and her capability in expression and the function of reaching for desires. Towards the end of the process, she showed a lot of activeness and agency in addition to growing power in expressing both “yes” and “no”.

The therapist encouraged Meryam to express her own wishes and thoughts by giving her possibilities and enough time to decide many of the details during the sessions (e.g., some decisions on the content of the sessions, the wish to walk the horse or not, or on the order of how different grooming acts with the horse were made), and by modelling a humorous, easy-going way of being and boldness in making bodily gestures. For example, in session VII, a joke emerged where Meryam gestured to the therapist that “I’ll go alone and you can stay there” when going to grab the gear from the saddle room and when walking the horse to the paddock.

From the beginning, Meryam also made a good reciprocal relationship with the horse, showing both tenderness and respect on one hand and determination on the other. In the therapeutic triangle of Meryam, the horse and the therapist, it became possible to model real-time reciprocal relationships, expressions and responsiveness: in session II the horse was itchy and expressed it, thus Meryam started to scratch her and ease her discomfort. The therapist also helped Meryam notice, for instance, how the horse, although standing still,

was following and listening to the movements of Meryam all the time, e.g., with her ears.

In sessions IX-X, it was also observed that Meryam somewhat pushed the horse away, not with anxiety or fear, but with mild disappointment towards the horse. For instance, Meryam approached the horse, but the horse turned her head away, with Meryam withdrawing herself with disappointment. This gave the therapist a possibility to model and guide Meryam for being able to just float in the feelings of sadness or disappointment without a quick withdrawal, thus giving new possibilities for rejoining together in communication. This resulted in the horse making contact towards Meryam where she could again join. The endings of the EFT sessions and saying goodbyes to the horse were especially fruitful moments in monitoring the feelings in the reciprocal relationship between Meryam and the horse.

With the horse it became also possible to model the act of refusing from something. For instance, in sessions IX-X Meryam started to tickle the horse's ear with good intentions, but which the horse did not like and turned her head away, and the therapist guided Meryam that the horse did not like it and that is something that has to be respected, ending up Meryam finding another way which the horse liked.

STRENGTHENING THE BODY-MIND INTEGRATION

First observation of Meryam's bodily control included somewhat looseness and imbalance on one hand (e.g., body pose and carriage when standing and walking), but at the same time some stiffness and tensions on the other (e.g., short steps and glancing to the ground when walking), in addition to many rather adequate bodily movements (e.g., hand movements and crouching when brushing the horse). When Meryam was riding the horse for the first time in session II, the body posture was very strained, sitting back with upper body leaning forward and the hip closed. Still in session V, when riding the horse for the second time, the body posture was very tensed up, stiff and unsteady. With continuing guidance from the therapist of breathing peacefully, stretching hands to the side and up to the sky, turning the torso back to scratch the horse's tail, instructing to open the chest and let the legs hang, Meryam's posture started session by session to relax and become more elastic and flexible.

In sessions X-XI, Meryam's bodily control had improved significantly: her hip had opened with relaxed legs hanging,

her back had risen to full length, her posture was stable, elastic and upright, yet relaxed. For instance, in session X, the horse started to move without warning and kicked at her stomach due to insects, but Meryam just sat with ease on her back with her body adjusting to the movements of the horse, whereas in the first sessions the same movements made her shaky, unstable and frightened, feeling like she was falling. As the ability to use speech to communicate and instruct was limited, the therapist used her own body to demonstrate and model movements of the hips, the torso and the hands (e.g., how the hip moves up-down, left-right and front-back with the pace of the walking horse).

Exercises were given to Meryam: closing her eyes while riding to let Meryam just feel the movements of the horse's gait, letting her body move with the pace of the horse, breathing peacefully and scanning the body with ease. The bodily exercises guided Meryam rather from just riding the horse to work on the area of body-mind integration and stabilizing the inner world. Thus, working with the mind-body integration also strengthened the regulation of fear and anxiety.

DISCUSSION

This case study aimed at describing and analysing a 12-week EFT process with a case of 13-year-old asylum seeker girl with PTSD. The EFT sessions were videotaped and analysed with the approach of grounded theory, which ended up forming three main categories of relevant emerging contents involving: 1) fear and anxiety regulation and widening the window of tolerance, 2) reciprocal expression of needs and desires and increasing of agency, and 3) strengthening the body-mind integration.

In summation, anxiety regulation was improved, the window of tolerance enhanced, agency increased and the body-mind integration strengthened by the EFT process. This was seen in the EFT sessions, as well as in the patient's real-life situations. During the sessions this was seen as a growing ability to approach and perform frightening acts and be more effective in self-calming, resulting in the maintenance of better inner calmness in situations where anxiety was raised, as stressed in the polyvagal theory. The other important follow-up, or means of evaluation, observations on how the things encountered in the stable transferred into the patient's everyday life were shown by the increasing functional capacity with things that were considered impossible or too frightening earlier. Whereas

prior to the process the patient was unable to go out alone due to fears and anxiety, towards the end of the process it became possible for her so that she was able, for instance, to go alone to school by train and bus, which was impossible for her before. No negative effects of the treatment were observed. This study had no follow-up, and that must be seen as a limitation, especially when the treatment period was rather short.

The horse was seen to play a crucial role in the whole process. Acting with the horse and in the stable environment made predisposing more possible than in a traditional psychotherapy setting: encountering frightening situations and real-time fear with the support of the therapeutic triangle and noticing that those can be encountered and survived. Most importantly, the horse acted as a force of attraction that motivated the patient to pull herself to the limits of her window of tolerance and to stretch it in order to be able to perform desired actions, such as to approach the horse, to mount the horse and to ride the horse. Thus, the horse motivated her to go towards things that felt frightening instead of escaping them. In the present case, caring for and riding the horse were the most effective means of activities in the stable to foster the desired psychological changes. In other cases, other contents of EFT can be the most effective ones, such as walking with the horse or cleaning the stable.

In this case, it was an advantage for the process that the patient came rather quickly, considering her traumatic history, into good, safe contact with the therapist and the horse. The good basic trust probably enabled and accelerated other therapeutic changes. The secure contact formation with the horse was nicely seen in session IX: the patient stated she was interested in approaching and walking another horse that had also been a small part of the process. She approached the other horse, but her anxiety grew so that she stopped and returned to the earlier horse to walk her. In this vignette, it can be seen how the relationship with the particular horse had grown during the process and how the horse acted as a safe haven for the patient. She reached for something interesting, but when the limit of the window of tolerance was crossed, she returned to find the ease for anxiety with the older horse. In addition, when the relationship with the horse had deepened, she showed great trust in the horse, for instance, when having the horse free in the corridor of the stable while tending her, without any halter. The referring psychotherapist who attended most of the sessions and who the patient already knew, also probably helped the contact form for Meryam with the therapist and the horse. All in all, it should be noted that this case got more attention than

usual, with e.g., the therapist transporting the girl to the stable and home, the familiar psychotherapist joining most of the sessions and the supervisor also joining two of the sessions. This extra effort by the professionals had probably some possible effect with the good outcome.

In addition, it is most important that, especially when treating patients with PTSD, the therapist offers and ensures enough safety in the therapeutic triangle and in the surroundings where there might occur many surprising and frightening situations for the patient. The therapist's calmness and both psychological and physical presence was important. The horse also needs to be suitable and trained for the EFT work. Thus, both the therapist and the horse need to be competent in offering enough safety for the patient all the time in the therapeutic triangle. Since the basic education of EFT therapists varies, the therapist should have a strong enough competence in mental health. The therapist needs also to know the individual horse well to be able to notice what the horse signals. The wellbeing of the horse should never be neglected. Excluding allergies, there are not that many contraindications since the stable environment offers many therapeutic possibilities, but, for instance, mistreating or aversion to animals could be among those.

One of the advantages in using EFT in treatment of a refugee or asylum seeker was observed with the rather small need for a shared spoken language. Whereas shared language is a key component in more traditional psychotherapy (at least via professional interpreter), in EFT, the desired changes in the psychological structures can be achieved by other means, such as in relation to the horse where speech is not needed. No major communication problems occurred in the present case, even though the patient spoke only very little Finnish. Picture cards used helped the communication in planning the sessions together with the patient, and the sign tables to word emotions during the process. Google Translator, used a little to "speak" in the car, worked well enough in this case. In a longer EFT process, it could be useful to have a more traditional session with a professional interpreter every now and then, mainly to name the psychological aspects of the process with the patient and to hear the patient's experiences or thoughts of the process. In the process of the present study, only the last home visit was used this way. EFT can also work as a parallel therapy alongside a more traditional speech-based psychotherapy, boosting the desired effects.

Communicating in the language of the new host country also has meaning from the perspective of integration into the new society and growing courage in general. Functioning together in the stable environment made it in this case less

pressuring to start to speak Finnish, even with very little vocabulary, thus lessening the feeling of insecurity and strengthening the thought of being able to speak without an interpreter. From there the experience can also manifest itself in other situations in everyday life. Communicating in Finnish also enhances courage in general to improvise and to throw oneself into situations with insecurity and to get experiences of capability.

However, it is very important that the therapist speaks only a little and with short clear sentences and takes into consideration how the patient feels when not understanding or when not being understood. It is also important to underline that the therapist also needs courage to communicate in other ways than speech, such as face and bodily expressions.

To conclude, with a case of an adolescent asylum seeker with PTSD, a 12-week EFT process was seen as a functioning method in working with patient's fears and anxiety towards better anxiety regulation, growing agency and body-mind integration. The present paper describes the process and its main contents and observations, stating that EFT can be used with this target group.

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Conflict of interest

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References

1. Castaneda, A. E., Junna, L., Lilja, E., Skogberg, N., Kuusio, H., Koponen, P., & Suvisaari J. (2017). The prevalence of potentially traumatic pre-migration experiences in Russian, Somali and Kurdish origin migrants in Finland: a population-based study in Finland. *Journal of Traumatic Stress Disorders and Treatment*, 6, 1.
2. Rask, S., Suvisaari, J., Koskinen, S., Koponen, P., Mölsä, M., Lehtisalo, R., Schubert, C., Pakaslahti, A., & Castaneda, A. E. (2016). The ethnic gap in mental health: a population-based study of Russian, Somali and Kurdish origin migrants in Finland. *Scandinavian Journal of Public Health*, 44, 281–290.
3. Castaneda, A. E., Snellman, O., Garoff, F., Klemettilä, A., Lehti, V., Qvarnström-Obrey, A.-C., Kankaanpää, S., Oroza, V., & Halla, T. (2019a). Järkyttävät tapahtumat ennen Suomeen tuloa. In: N. Skogberg, K.-L. Mustonen, P. Koponen, P. Tiittala, E. Lilja, A. Ahmed Haji Omar, O. Snellman, A. E. Castaneda (Eds.), *Turvapaikanhakijoiden terveys ja hyvinvointi. Tutkimus Suomeen vuonna 2018 tulleista turvapaikanhakijoista. Raportti, 12. Publications of the Finnish Institute for Health and Welfare.*
4. Castaneda, A. E., Snellman, O., Garoff, F., Klemettilä, A., Lehti, V., Qvarnström-Obrey, A.-C., Kankaanpää, S., Oroza, V., & Halla, T. (2019b). Psykkiset oireet. In: N. Skogberg, K.-L. Mustonen, P. Koponen, P. Tiittala, E. Lilja, A. Ahmed Haji Omar, O. Snellman, A. E. Castaneda (Eds.), *Turvapaikanhakijoiden terveys ja hyvinvointi. Tutkimus Suomeen vuonna 2018 tulleista turvapaikanhakijoista. Raportti, 12. Publications of the Finnish Institute for Health and Welfare.*
5. Lentini, J. A., & Knox, M. S. (2015). Equine-facilitated psychotherapy with children and adolescents: An update and literature review. *Journal of Creativity in Mental Health*, 10, 278–305.
6. O’Haire, M. E., Guérin, N. A., & Kirkham, A. C. (2015). Animal-assisted intervention for trauma: A systematic literature review. *Frontiers in Psychology*, 6, 1121.
7. Nevins, R., Finch, S., Hickling, E. J., & Barnett, S. D. (2013). The Saratoga WarHorse project: A case study of the treatment of psychological distress in a veteran of operation Iraqi freedom. *Advances in Mind-Body Medicine*, 27, 22–25.
8. Wharton, T., Whitworth, J., Macauley, E., & Malone, M. (2019). Pilot testing a manualized equine-facilitated cognitive processing therapy (EF-CPT) intervention for PTSD in veterans. *Psychiatric Rehabilitation Journal*, 42, 268–276.
9. Kemp, K., Signal, T., Botros, H., Taylor, N., & Prentice, K. (2014). Equine facilitated therapy with children and adolescents who have been sexually abused: A program evaluation study. *Journal of Child and Family Studies*, 23, 558–566.
10. McCullough, L., Riskey-Curtiss, C., & Rorke, J. (2015). Equine facilitated psychotherapy: A pilot study of effect on posttraumatic stress symptoms in maltreated youth. *Journal of Infant, Child, and Adolescent Psychotherapy*, 14, 158–173.
11. Naste, T. M., Price, M., Karol, J., Martin, L., Murphy, K., Miguel, J., & Spinazzola, J. (2018). Equine Facilitated Therapy for Complex Trauma (EFT-CT). *Journal of Child & Adolescent Trauma*, 11, 289–303.
12. Signal, T., Taylor, N., Botros, H., Prentice, K., & Lazarus, K. (2013). Whispering to horses: Childhood sexual abuse, depression and the efficacy of equine facilitated therapy. *Sexual Abuse in Australia and New Zealand*, 5, 24–32.
13. Yorke, J., Nugent, W., Strand, E., Bolen, R., New, J., & Davis, C. (2013). Equine-assisted therapy and its impact on cortisol levels of children and horses: A pilot study and meta-analysis. *Early Child Development and Care*, 183, 874–894.

14. Castaneda, A. E., Mäki-Opas, J., Jokela, S., Kivi, N., Lähteenmäki, M., Miettinen, T., Nieminen, S., Santalahti, P. & PALOMA-asiantuntijaryhmä. (2018). Pakolaisten mielenterveyden tukeminen Suomessa. PALOMA-käsikirja. Ohjaus, 5. Publications of the Finnish Institute for Health and Welfare.
15. Porges, S. W. (2011). The polyvagal theory. Neurophysiological foundations of emotions, attachment, communication, self-regulation. WW Norton & Company.
16. Dana, D. (2018). The polyvagal theory in therapy. Engaging the rhythm of regulation. WW Norton & Company.
17. Leikola, A., Mäkelä, J., & Punkanen, M. (2016). Polyvagaalinen teoria ja emotionaalinen trauma. *Duodecim*, 132, 55–61.
18. Strauss, A., & Corbin, J. M. (1990). *Basics of qualitative research: Grounded theory procedures and techniques*. Sage Publications Inc.



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ADOLESCENTS WITH SEVERE DEPRESSIVE AND ANXIETY DISORDERS – A NATIONWIDE REGISTER STUDY OF INPATIENT-TREATED ADOLESCENTS 1980- 2010

ABSTRACT

Objective: To explore trends in the inpatient treatment of adolescent internalizing disorders, namely depressive and anxiety disorders. To compare the prognosis of these disorders regarding readmissions, diagnostic stability, mortality, and symptom severity and functioning with similar indices among adolescents psychiatrically hospitalized due to other disorders.

Materials and methods: A register-based follow-up study of all adolescents with their first ever psychiatric admission at ages 13-17 in the period 1980-2010.

Results: The number and proportion of internalizing disorders as primary diagnoses in the psychiatric inpatient care of adolescents increased vastly across decades, particularly among girls. Readmissions, mortality and symptom severity and functioning did not essentially differ from those with other diagnoses and did not essentially improve over time.

Conclusions: Our findings do not lend support to the assumption that increased treated incidence of adolescent internalizing disorders is due to medicalization.

KEYWORDS: ADOLESCENT, DEPRESSION, ANXIETY DISORDERS, HOSPITALIZATION

INTRODUCTION

Depression and anxiety are among the most common internalizing disorders during adolescence [1]. Almost one third of adolescent boys and over half of girls self-report potentially clinically significant symptoms of depression or anxiety disorder at some point during adolescence [2]. In a meta-analysis of studies from 27 countries, the point prevalence of depressive disorder in a community sample under 18 years of age was 2.6% and that of anxiety disorder was 6.5% [3]. The systematic review also included children which lowers the point prevalence compared to studies including only adolescents. In a large US National Comorbidity Study, the lifetime incidence of depressive disorder in an adolescent community sample was 11.7%, and of anxiety disorders 31.9%; incidences of disorders with severe impairment were 8.7% for depressive and 8.3% for anxiety disorders [4].

Of adolescents with depressive disorders, up to 75% present with comorbid anxiety disorder and it is estimated that 10-15% of adolescents with primary anxiety disorders meet the criteria for depressive disorder [5,6]. Left untreated, a psychiatric disorder at a young age poses a serious threat to adolescent development [7]. A link to poorer school performance and quality of life has been found in a study based on Finnish data for both depression and anxiety disorder. Long-term and severe symptoms as well as comorbidities increase the risk of adverse consequences [8]. The number of mental disability pensions among Finnish young people has increased. Depression is the most common disorder underlying the disability pension for persons aged 16–34. During the period 2015-2019, pensions related to anxiety disorder also became more common in all age groups, especially in women [9].

Psychiatric hospital care for adolescents is targeted at patients with severe symptoms and significant dysfunction, or at the risk of harming themselves or others [10]. Between 1980 and 2010, health policies promoted adolescent psychiatric care, and the number of psychiatric inpatient beds for adolescents and the number of young people admitted to psychiatric hospital care increased vastly in Finland [11], also reported elsewhere. At the same time, the proportion of girls in hospital care increased, associated with an increase in proportion of diagnoses more common among girls than boys, such as depression and anxiety disorder. Among adolescent psychiatric inpatients in Finland, the proportion of those with a diagnosis of depression increased from 25%

to 38%, and that of patients with anxiety disorder from 8% to 19%, between 2000 and 2011 [12].

The mental health status of young people treated in psychiatric hospital care has been described as having become more severe over time [12,13]. Readmission is a commonly used indicator of prognosis in inpatient care. The number of young people readmitted for psychiatric inpatient treatment less than six months from discharge is approximately 12.1-28%. Risk factors for the new hospital stay among adolescents include psychiatric comorbidity, somatic chronic diseases and number of earlier admissions [14]. In adolescents with depression, faster rehospitalization has been associated with self-injury without suicidal intent [15]. In an earlier study based on our data, 40% of young people returned to hospital at least once between the ages of 13 and 17. Of patients treated for mood disorders (F30-39), 41% were readmitted, of patients with neurotic, stress-related and somatoform disorders (F40-49), 39% [11].

The incidence of many mental disorders, including depression and anxiety disorder, peaks in adolescence and young adulthood [1,16]. Psychiatric disorder at a young age increases the risk of adult psychiatric disorder at least threefold [17]. Further, a persistent or recurrent disorder in adolescence predicts more psychiatric problems in adulthood [18]. Homotypic continuity refers to the recurrence of the primary disorder as the same disorder in later life [1,17,19]. In turn, heterotypic continuity characterizes a situation where morbidity continues but subsequent manifestation differs from the primary diagnosis. Homotypic and heterotypic continuity can also be studied in the level of higher order dimensions (internalizing disorders, externalizing disorders) [19]. The recurrence of psychiatric disorders among young people is mainly homotypic, but diagnostic crossover occurs, particularly between depression and anxiety disorders. In other words, depression in adolescence predicts subsequent anxiety disorder and vice versa [1,17,19].

Adolescent psychiatric disorder increases the long-term risk of premature mortality [20,21,22]. Among adults, depression alone has been shown in several studies to increase the risk of death [23,24,25], and the connection appears to be stronger for men than for women [25,26,27,28]. The occurrence of anxiety disorder with depression appears to reduce mortality in depressed adult patients [25,29,30], and anxiety disorder alone does not appear to be related to increased risk of mortality [24,29,31]. However, to the best of our knowledge, research has not focused specifically on mortality in adolescent-onset depression and/or anxiety disorders.

In 2020, the proportion of suicides among total causes of death in Finnish adolescents was 26% [32]. On average, psychiatric hospitalization is associated with an eight-fold increased risk of suicide [33]. Of adolescent psychiatric hospital-treated patients, 17–55% have attempted suicide [34]. Comorbidity of depression and anxiety disorder increases the risk of suicide in adolescents [31].

AIMS OF THE STUDY

Depression and anxiety are the core internalizing disorders. Their prevalence is high among adolescents. These disorders are often comorbid and predict each other's incidence. Given that the number of adolescents hospitalized due to these disorders has vastly increased in recent decades [11], they have considerable economic implications.

Finnish registers afford the opportunity to scrutinize the psychiatric morbidity of Finnish adolescents over a long period of time. To increase the understanding of the increasing needs related to adolescent depression and anxiety disorders, we set out to study rehospitalizations, homotypic and heterotypic continuity of diagnoses and mortality among adolescents hospitalized for these disorders in the period 1980–2010. We intend to examine whether the incidence of depression and anxiety disorders requiring hospitalization has changed from the 1980s to the 21st century, and what the outcome is like for patients who have been hospitalized for depression and anxiety disorder in terms of symptom severity, rehospitalization, continuity and mortality.

METHODS

The study is a register-based follow-up study based on comprehensive nationwide data. Finland's comprehensive and reliable patient registers together with personal ID numbers enable the processing of large amounts of patient data and the compilation of data. As a basis for information on inpatient care we used the Hospital Discharge Register and the Care Register for Health Care, both kept by the Finnish Institute for Health and Welfare. The variables used are the dates of admission and discharge, the patient's sex, age, the initial and end dates of any new hospital treatment, and the diagnoses during the index treatment period and subsequent treatment periods. Symptom severity was described by GAS registered at admission. In addition, cause of death data was extracted from the

Mortality register (Statistics Finland) for subjects who died during the follow-up period. The original data included those 13 to 17-year-olds who received psychiatric hospital care for the first time in the period 1980–2010. The data were extracted by register keepers and pseudonymized by Statistics Finland. All in all, these criteria included 17,112 young people on the register. There were 40.2% (6,873) boys and 59.8% (10,239) girls in the data. During their first treatment, 270 of them did not receive a psychiatric or neurological diagnosis and were thus excluded, resulting in a final analysable sample of 16,842 patients. Patients were followed up in registers for up to ten years or until 2014 or death, whichever criterion came first.

The data contain diagnostic data from three different ICD (International Classification of Diseases) classifications used at different times. ICD-8 was used in Finland between 1968 and 1986, ICD-9 from 1987 to 1995, and ICD-10 has been in use since 1996. The WHO conversion patterns were used to modify the ICD-8 and ICD-9 diagnostics to follow the ICD-10 classification. The primary diagnosis in the registry was set to describe the main cause of hospitalization. Our research focuses on diagnostic codes F32–33 for depressive disorders and F40–48 for anxiety disorders. In this study we use the term internalizing disorders to refer to both these disorders together. In studying diagnostic stability, internalizing disorders were combined, mania and bipolar disorder (F30 and F31) were grouped together, and other diagnoses were used as categorized to main categories (F00–09, F10–19, F20–29...).

GAS (Global Assessment Scale) is a method of evaluation to monitor the change in the patient's ability to function and to define the objectives of rehabilitation for a specific period. The scale ranges from 1 to 100, with lower scores indicating greater symptom severity. GAS has been found to be reliable as an assessment method (35). It is now compulsory in Finland to register GAS at the beginning and at the end of psychiatric hospitalization. The values are determined by the treating physician according to the instructions of the Finnish Institute for Health and Welfare. A GAS assessment of the patient's mental status has been available from the registry at the beginning and end of the treatment period since 1996, and thus the arrival GAS assessments are used in the present study for a subsample admitted since 1996.

STATISTICAL ANALYSES

The data were analysed by statistical methods for quantitative data. Patients treated for internalizing disorders were compared with patients treated for other disorders. The groups were compared by cross-tabulation and the statistical significance was examined by Chi-square test (Fisher's exact test where appropriate). The number and proportion of patients hospitalized due to internalizing disorders were also compared according to the sex and phase of adolescent development and between the various decades (1980—1989, 1990—1999, 2000—2010). Readmissions and diagnostic stability were compared between internalizing and other disorders in different decades. Differences in mortality were likewise explored between internalizing and other disorders by sex, age at index admission (13-14-year-olds (early adolescence) vs. 15-17-year-olds (middle adolescence)) and decade. Causes of death were compared between the diagnostic groups (internalizing vs. others). From 1996, admission GAS estimates were compared between internalizing and other disorders. Within the group of internalizing disorders, we compared the incidence of depression and anxiety and likewise readmissions, diagnostic stability and mortality. Due to the large data size, the cut-off for statistical significance was set at $p < 0.001$.

RESULTS

INCIDENCE BETWEEN 1980 AND 2010

Internalizing disorder as a primary diagnosis during the first hospitalization period was across the decades more common among girls than boys. Internalizing disorder as a reason for the index admission was equally common in early and mid-adolescent patients (13–14-year-old boys 35.2% and 15–17-year-old boys 36.6%, $p=0.2$; 13–14-year-old girls 51.0% and 15–17-year-old girls 51.9%, $p=0.4$). The share of internalizing disorders as the main diagnosis increased significantly among both boys and girls from decade to decade. In absolute terms, the number of patients treated for these disorders more than tripled in boys and increased ninefold in girls (Table 1). Of the internalizing disorders at the index admission, 53.9% (4191/7773) were depressive disorders, 37.4% (2908) anxiety disorders and 8.7% (674) comorbid depression and anxiety.

In the internalizing disorders group, the preponderance of anxiety disorders in the 1980s changed to a preponderance of depressive disorders in the 2000s. This was seen in both sexes (Table 2).

Table 1. Proportions and numbers of internalizing disorders (F32-39, F40-49) as primary diagnoses among adolescents admitted for psychiatric inpatient treatment for the first time between the ages of 13 and 17 in 1980-2010 (%(n/N))

	Total	Boys	Girls	p (between sexes)
1980–2010	45.4% (7773/17112)	36.2% (2485/6873)	51.6% (5288/10239)	<0.001
1980–1989	33.7% (871/2588)	30.7% (430/1401)	37.2% (441/1187)	0.001
1990–1999	40.4% (1455/3604)	36.4% (580/1594)	43.6% (875/2008)	<0.001
2000–2010	49.9% (5447/10922)	38.0% (1475/3878)	56.4% (3972/8044)	<0.001
p (between decades)	<0.001	<0.001	<0.001	

Table 2. Distribution of main diagnoses among internalizing disorders in adolescents with first psychiatric hospitalization at ages 13-17 in 1980–2010 (n (%))

		Boys	Girls	p (between sexes)	Total
Boys	F32-39	19.1% (82)	37.8% (219)	61.2% (902)	48.4% (1203)
	F40-48	80.9% (348)	62.2% (361)	38.8% (573)	51.6% (1282)
Girls	F32-39	23.4% (103)	51.0% (446)	71.2% (2827)	63.8% (3376)
	F40-48	76.6% (338)	49.0% (429)	28.8% (1145)	36.2% (1912)
Total	F32-39	21.2% (185)	45.7% (665)	68.5% (3729)	58.9% (4579)
	F40-48	78.8% (686)	54.3% (790)	31.5% (1718)	41.1% (3194)

NEED FOR REHOSPITALIZATION AND DIAGNOSTIC STABILITY

More than half of those treated for internalizing disorders during the first hospitalization were later readmitted. However, in the case of other disorders, the probability of rehospitalization was statistically significantly higher than in the case of internalizing disorders, although the absolute difference in percentages was small (Table 3). In a decade stratified analysis, the proportions of rehospitalizations did not systematically differ between patients treated for internalizing disorders and for other disorders (1980–1989, p=0.3; 1990–1999, p=0.02; 2000–2010, p=0.08).

Diagnostic stability was explored by comparing the primary diagnosis of the initial internalizing disorder to the primary diagnosis in the most recent hospitalization period during the ten years of follow-up among those who had at least one rehospitalization. In total, 4,116 patients were rehospitalized, among whom the primary diagnosis of internalizing disorder remained unchanged (57.5%). In boys, the persistence of an internalizing diagnosis was statistically significantly lower than in girls (boys 52.6%; girls 59.8%; p<0.001). Between the decades, the diagnostic

stability of internalizing disorders increased (1980-1989 45.4%; 1990-1999 53.2%; 2000-2010 61.3%; p<0.001). Age at index admission had no impact on diagnostic stability. In boys the diagnostic change, if present, was more in the direction of schizophrenic group psychoses (F20-29) or intellectual disabilities/other developmental disorders of speech and language (F70-79/F80-89). In girls, if diagnostic changes occurred, the initial internalizing diagnoses most commonly changed to bipolar disorder.

Within the internalizing disorder group, rehospitalization was equally common among patients with primary diagnosis of depression and anxiety disorder, both in boys and girls, and in early and middle adolescents, but decreased across the decades. In the latest decade, the risk of rehospitalization was higher in patients with depression than in patients with anxiety disorder (Table 4).

Table 3. Proportion of patients rehospitalized during a follow-up of 10 years by main diagnostic group (%(n/N))

	Internalizing disorders (F32-39, F40-49)	Other psychiatric disorders	p
Boys	53.7% (1334/2485)	56.9% (2495/4388)	0.011
Girls	52.6% (2782/5288)	56.4% (2790/4951)	<0.001
Total	53.0% (4116/7773)	56.6% (5285/9339)	<0.001

Table 4. Proportion of patients rehospitalized during ten years of follow-up by primary diagnosis in the internalizing group (%(n/N))

	F32-39	Other psychiatric disorders	p
1980–89	63.2% (117/185)	62.8% (431/686)	0.92
1990–99	60.8% (404/665)	57.3% (453/790)	0.19
2000–2010	52.1% (1941/3729)	44.8% (770/1718)	<0.001

MORTALITY

During the ten-year follow-up period, 2.4% (N=290/7773) of those treated for an internalizing disorder at index admission had died, of patients treated for other disorders, 3.2% (N=295/9339) (p=0.005). Mortality in the internalizing disorder group did not differ from mortality in patients treated for other diagnoses when analyses were stratified by sex (in boys: 4.3% vs. 4.5%, p=0.7; in girls: 1.6% vs. 2.0%, p=0.1), but male mortality was higher than female mortality in both internalizing and comparison groups (p<0.001).

Among those admitted to their index admission period in early adolescence there was no difference in mortality comparing the primary diagnosis of internalizing disorder to other disorders. Whereas among those first admitted as middle adolescents, internalizing disorders were associated with lower mortality in follow-up than other primary diagnoses (2.7% vs. 3.9%, p=0.001). In the internalizing

disorder group, mortality was similar in the depressive and anxiety disorder groups.

Among the deceased, cause of death was suicide in 52%, accidents and violence in 31% and natural causes in 17%. There were no statistically significant differences in the distribution of causes of death by diagnostic group in the whole sample or in the sex and decade-specific analyses.

GAS SCORE

Mean GAS at index admission among patients treated for internalizing disorders was similar to that in patients treated for other disorders and did not improve over time, even if the number of patients admitted increased (Figure 1). In the anxiety disorder group, GAS mean levels were slightly higher in the 1990s than in the depression group, but the difference diminished towards the end of the period scrutinized (Figure 2).

Figure 1. Mean GAS at admission to index inpatient period: patients with internalizing disorders compared to all other patients

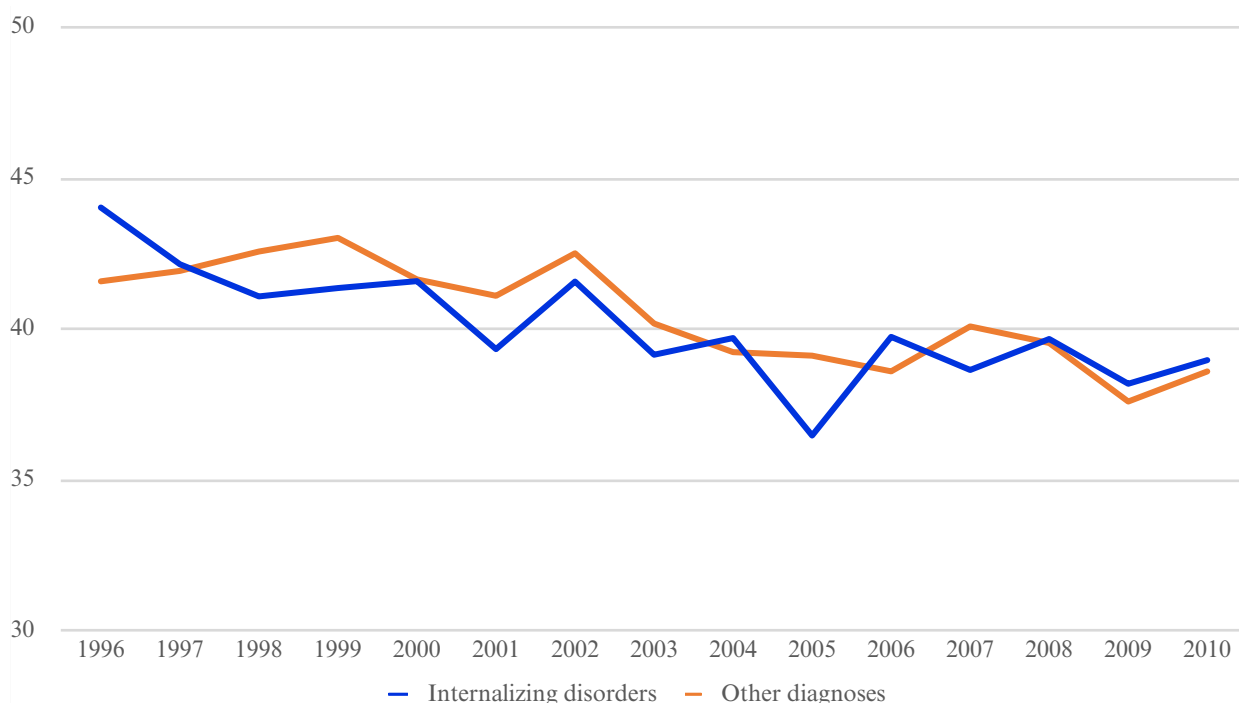
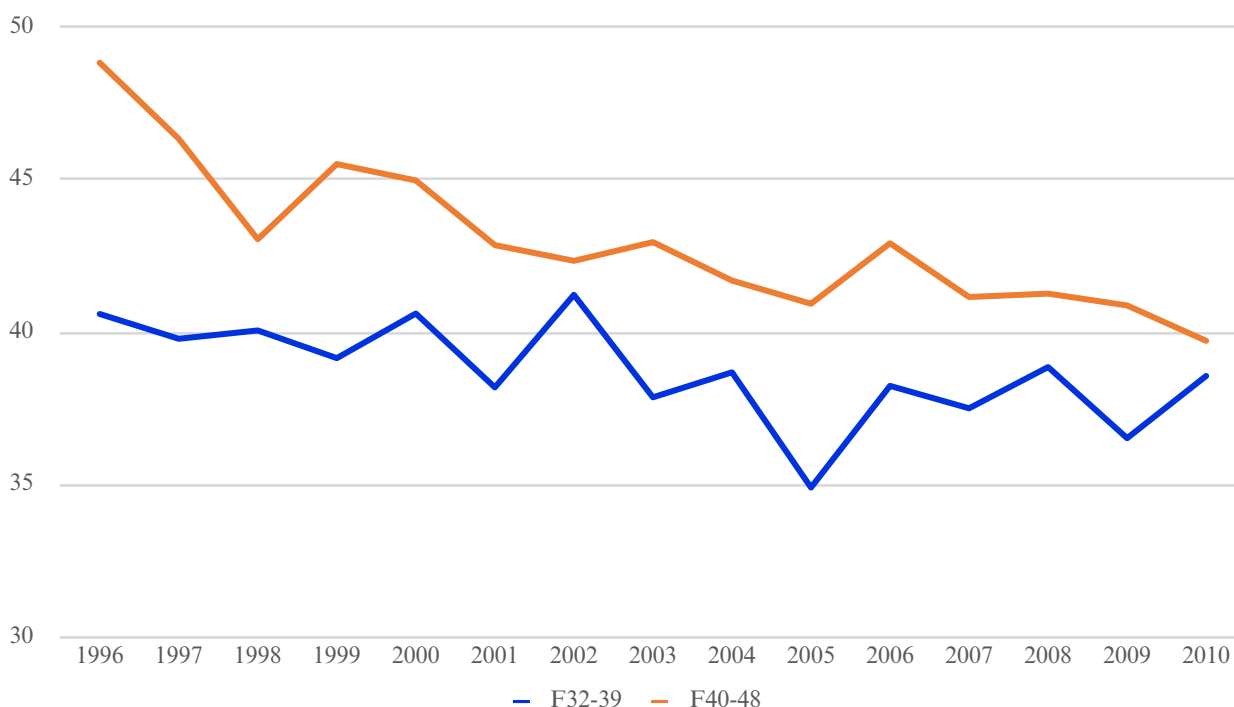


Figure 2. Mean GAS at admission to index inpatient period among the two internalizing groups



DISCUSSION

Among adolescents with their first ever psychiatric admission at ages 13-17 in the period 1980-2010, the absolute number and proportion of all admissions with a main diagnosis of internalizing disorders (F32-29, F40-49) increased vastly from the 1980s to the 2000s. The proportion and mortality of rehospitalized patients were slightly lower in the group of internalizing disorders than in those treated for other disorders. These indicators did not change over time. The primary diagnosis of internalizing disorder in the first hospitalization period persisted in more than half of the new inpatient treatment cycles, and diagnostic stability increased over time. Even if the number of adolescents admitted for internalizing disorders increased, GAS assessment suggested very little change in their symptom severity and functioning across the decades. If anything, GAS scores worsened, and did not differ from those of patients treated for other disorders.

In absolute terms, the incidence of internalizing disorders requiring hospitalization tripled in boys and increased ninefold in girls in the period scrutinized. However, there were no changes in the overall incidence of internalizing symptoms among adolescents based on either international

meta-analyses or on the Finnish population survey [36,37,38]. Internalizing disorder as a primary diagnosis in the first hospitalization period was more common in girls than in boys in all the decades considered, which concurs with known sex differences in these disorders [2]. The known sex differences in morbidity do not, however, explain why being hospitalized because of these disorders continued to increase in girls more than in boys. Nevertheless, the amount of treatment provided has earlier been insufficient in relation to morbidity. During the study period, the need may have been met better but still probably not well enough. According to more recent Finnish community sample studies, the incidence of adolescent internalizing symptoms may be increasing [39,40]. This may further increase the need for inpatient treatment.

Half of those treated for a primary diagnosis of depression or anxiety disorder during their first psychiatric hospitalization were rehospitalized during a ten-year follow-up period, slightly less than those treated for other disorders. This would suggest that internalizing disorders requiring hospitalization in adolescence are quite serious and require long-term specialized medical care. The proportion of rehospitalized patients in the internalizing disorder group decreased slightly over time. This may be due to a lowering

of the threshold to inpatient care, but also to improvements in the effectiveness of outpatient care.

Continuity of psychiatric morbidity among young people has previously been found to be mainly homotypic [1,17,19]. In these data, the diagnosis of internalizing disorder persisted in 57% of new treatment cycles and the diagnostic stability increased towards the present. The more marked persistence of diagnoses in later cohorts may be explained by changes in diagnostic classifications and evolving diagnostic practices. Interest in better diagnostics in depressive disorders was increased by the introduction to the market of SSRIs in the early 1990s [41] and may play a role here. The change in the proportions of depression and anxiety disorders within the group of internalizing disorders could also be related to the introduction of SSRIs and the increased precision in depression diagnostics. In 1980-1999, primary diagnosis of anxiety disorder was more common than depression in both girls and boys and young and older adolescents. In the 21st century, the proportions were reversed. Of course, it is also possible that there has been a change in the actual symptom picture in a more depressed direction.

Internalizing disorders were not only more common in girls than in boys; persistence of the diagnosis was also more stable in girls. This may indicate greater challenges in diagnostic work among adolescent boys. In boys, the change in diagnosis happened more frequently towards the group of schizophrenic psychoses, while in girls the change occurred more in the bipolar direction. Bipolar disorder is diagnostically closer to depression and anxiety disorders, which serves to confirm the potential diagnostic challenges for boys. In boys, a greater share of internalizing type of symptom presentation may actually represent the prodrome of psychosis.

The mortality rate among adolescents treated in hospital due to internalizing disorders did not differ from that of adolescents hospitalized due to other disorders. Nor were there any changes in mortality over time or any differences observed when comparing depression to anxiety disorders. These findings do not suggest a lowering of the threshold to inpatient care due to internalizing disorders over time. Adolescents hospitalized due to depressive and anxiety disorders represent a seriously ill proportion of the young. This is further underlined by noticing that their mortality did not decrease over time, even if suicide mortality in general has been in steady decrease over the study period and beyond in Finland [42]. On the other hand, based on our data, the mortality rate among young people with psychiatric disorders in need of hospital care does not appear to be

heavily dependent on the disorder itself, but it is more likely dependent on the severity of the disorder.

Mortality in boys was higher than in girls. This is consistent with results reported among adults [25,26,27] and sex differences in mortality in general population [43]. GAS scores for hospital patients were available from 1996. There was no discernible difference in GAS between internalizing disorders and other disorders, and no improvement between the 1990s and 2010s in either group. This does not indicate a lowering of the hospital admission threshold.

The number of adolescent depression and anxiety patients in psychiatric hospital care has increased sharply from one decade to the next, especially in the 21st century. No similar increase in the incidence of these disorders at population level has been demonstrated. The incidence of rehospitalizations among adolescent patients due to depression and anxiety disorders has been almost as high as among patients treated for other psychiatric disorders. In addition, their ability to function has been as low as those treated for other disorders and the proportion of people assigned to a new hospital cycle has decreased only slightly. These findings do not suggest that the increasing number of young people with depression and anxiety disorders in hospital care has to do with the growth pains of youth and psychiatric disorders, i.e., medicalization.

The need for treatment is influenced by several factors other than the incidence and severity of the disorder. These may include various social factors and increasing demands in the lives of young people, in the family, at school and at community level. The general acceleration of the pace of life and the increased use of social media have been proposed as risk factors for young people's internalizing disorders [44,45]. In addition, the role of social and cultural risk factors may be different for girls and boys, and even the role of biological and hormonal factors for differences in mental health epidemiology remains yet unresolved.

METHODOLOGICAL CONSIDERATIONS

The strength of our research is that it is based on a comprehensive, national register over three decades. National registry data allow reliable analysis and comparison of data on adolescent psychiatric hospital patients. However, the register does not take into consideration regional differences in the implementation and availability of psychiatric care. In addition, the diagnostics of the registry are based on clinical data, which could lead to diagnostic uncertainty. Psychiatric diagnostics in Finland,

however, have previously been found to be reliable in psychiatric hospital care [46]. A registry-based study only allows for the examination of more general phenomena. A more detailed analysis would require an examination of individual patient data. Therefore, several known risk factors such as genetics, socio-economic family background and the significance of adverse childhood experiences (ACEs) were not included in the study.

Unfortunately, the GAS scores were only available from 1996. The possibility of a GAS comparison before 1996 would also have been valuable because a change in the number of hospitalizations occurred specifically in the mid-1990s [11].

CONCLUSION

The number of adolescent patients hospitalized for depression and anxiety disorder increased markedly from the 1980s to the 2000s. The functional capacity of hospitalized depression and anxiety patients was as weak as that of inpatients treated for other psychiatric disorders and remained similar as the number of inpatients increased. The prognosis of internalizing disorders in light of rehospitalization periods and mortality was similar to that of other disorders requiring hospitalization. There appears to be no evidence that medicalization could explain the increasing need for adolescent psychiatric hospital care. Treatment of depression and anxiety disorders in adolescents should be intensified at all levels of treatment. The causes for greater increases in treated incidence of internalizing disorders in girls remain unclear.

Disclosure statement

The authors declare that they have no conflicts of interest.

Ethical approval

The study was duly approved by the ethics committee of Tampere University Hospital, and data extraction and use in research was approved by the Finnish Institute for Health and Welfare and Statistics Finland.

Author contributions

All authors contributed to the study conception and design. Data preparation and analysis were performed by Timo Holttinen. The first draft of the study was written by Jutta Niemi and all authors commented on previous versions. All authors read and accepted the final draft.

Data availability statement

Availability of datasets used and/or analysed in this study is subject to data permits from the Finnish register authorities. T.H. will provide further information at readers' requests.

Additional information

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References

1. Costello EJ, Copeland W, Angold A. Trends in psychopathology across the adolescent years: what changes when children become adolescents, and when adolescents become adults? *J Child Psychol Psychiatry*. 2011 Oct;52(10):1015-25. doi: 10.1111/j.1469-7610.2011.02446.x
2. Patton GC, Coffey C, Romaniuk H, Mackinnon A, Carlin JB, Degenhardt L, Olsson CA, Moran P. The prognosis of common mental disorders in adolescents: a 14-year prospective cohort study. *Lancet*. 2014 Apr 19;383(9926):1404-11. doi: 10.1016/S0140-6736(13)62116-9
3. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *J Child Psychol Psychiatry*. 2015 Mar;56(3):345-65. doi: 10.1111/jcpp.12381
4. Merikangas KR, He JP, Burstein M, Swanson SA, Avenevoli S, Cui L, Benjet C, Georgiades K, Swendsen J. Lifetime prevalence of mental disorders in U.S. adolescents: results from the National Comorbidity Survey Replication--Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry*. 2010 Oct;49(10):980-9. doi: 10.1016/j.jaac.2010.05.017
5. Karlsson L, Pelkonen M, Ruutu T, Kiviruusu O, Heilä H, Holi M, Kettunen K, Tuisku V, Tuulio-Henriksson A, Törrönen J, Marttunen M. Current comorbidity among consecutive adolescent psychiatric outpatients with DSM-IV mood disorders. *Eur Child Adolesc Psychiatry*. 2006 Jun;15(4):220-31. doi: 10.1007/s00787-006-0526-7
6. Cummings CM, Caporino NE, Kendall PC. Comorbidity of anxiety and depression in children and adolescents: 20 years after. *Psychol Bull*. 2014 May;140(3):816-45. doi: 10.1037/a0034733
7. Aalto-Setälä T, Marttunen M. Nuoren psyykinen oireilu--häiriö vai normaalia kehitystä? *Duodecim*. [Internet]. 2007;123(2):207-13. Finnish. Available: <https://www.duodecimlehti.fi/duo96233>

8. Kasteenpohja T, Marttunen M, Aalto-Setälä T, Perälä J, Saarni SI, Suvisaari J. Outcome of depressive and anxiety disorders among young adults: Results from the Longitudinal Finnish Health 2011 Study. *Nord J Psychiatry*. 2018 Apr;72(3):205-213. doi: 10.1080/08039488.2017.1418429
9. Laaksonen M, Blomgren J, Perhoniemi R. Mielenterveyssyistä alkavat eläkkeet ovat yleistyneet nuorilla mutta vähentyneet vanhemmissa ikäryhmissä. *Lääkärilehti*. [Internet]. 36/2021 vsk 76s. 1889 – 1897. Available: <https://www.laakarilehti.fi/tieteessa/alkuperaistutkimukset/mielenterveyssyista-alkavat-elakkeet-ovat-yleistyneet-nuorilla-mutta-vahentyneet-vanhemmissa-ikaryhmissa/>
10. Evans N, Edwards D, Carrier J. Admission and discharge criteria for adolescents requiring inpatient or residential mental health care: a scoping review. *JBIS Synth*. 2020 Feb;18(2):275-308. doi: 10.11124/JBISRIR-2017-004020
11. Holttinen T, Pirkola S, Rimpelä M, Kaltiala R. Factors behind a remarkable increase in adolescent psychiatric inpatient treatment between 1980 and 2010 - a nationwide register study. *Nord J Psychiatry*. 2021 Jun 29;1-9. doi: 10.1080/08039488.2021.1939780
12. Kronström K, Ellilä H, Kuosmanen L, Kaljonen A, Sourander A. Changes in the clinical features of child and adolescent psychiatric inpatients: a nationwide time-trend study from Finland. *Nord J Psychiatry*. 2016 Aug;70(6):436-41. doi: 10.3109/08039488.2016.1149617
13. Case BG, Olfson M, Marcus SC, Siegel C. Trends in the inpatient mental health treatment of children and adolescents in US community hospitals between 1990 and 2000. *Arch Gen Psychiatry*. 2007 Jan;64(1):89-96. doi: 10.1001/archpsyc.64.1.89
14. Phillips MS, Steelesmith DL, Campo JV, Pradhan T, Fontanella CA. Factors Associated with Multiple Psychiatric Readmissions for Youth with Mood Disorders. *J Am Acad Child Adolesc Psychiatry*. 2020 May;59(5):619-631. doi: 10.1016/j.jaac.2019.05.024
15. van Alphen NR, Stewart JG, Esposito EC, Pridgen B, Gold J, Auerbach RP. Predictors of Rehospitalization for Depressed Adolescents Admitted to Acute Psychiatric Treatment. *J Clin Psychiatry*. 2017 May;78(5):592-598. doi: 10.4088/JCP.15m10326
16. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005 Jun;62(6):593-602. doi: 10.1001/archpsyc.62.6.593
17. Copeland WE, Adair CE, Smetanin P, Stiff D, Briante C, Colman I, Fergusson D, Horwood J, Poulton R, Costello EJ, Angold A. Diagnostic transitions from childhood to adolescence to early adulthood. *J Child Psychol Psychiatry*. 2013 Jul;54(7):791-9. doi: 10.1111/jcpp.12062
18. Colman I, Wadsworth ME, Croudace TJ, Jones PB. Forty-year psychiatric outcomes following assessment for internalizing disorder in adolescence. *Am J Psychiatry*. 2007 Jan;164(1):126-33. doi: 10.1176/ajp.2007.164.1.126
19. Shevlin M, McElroy E, Murphy J. Homotypic and heterotypic psychopathological continuity: a child cohort study. *Soc Psychiatry Psychiatr Epidemiol*. 2017 Sep;52(9):1135-1145. doi: 10.1007/s00127-017-1396-7
20. Archer G, Kuh D, Hotopf M, Stafford M, Richards M. Adolescent affective symptoms and mortality. *Br J Psychiatry*. 2018 Jul;213(1):419-424. doi: 10.1192/bjp.2018.90. Epub 2018 May 28
21. Jokela M, Ferrie J, Kivimäki M. Childhood problem behaviors and death by midlife: the British National Child Development Study. *J Am Acad Child Adolesc Psychiatry*. 2009 Jan;48(1):19-24. doi: 10.1097/CHI.0b013e31818b1c76

22. Maughan B, Stafford M, Shah I, Kuh D. Adolescent conduct problems and premature mortality: follow-up to age 65 years in a national birth cohort. *Psychol Med*. 2014 Apr;44(5):1077-86. doi: 10.1017/S0033291713001402
23. Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. *Am J Psychiatry*. 2014 Apr;171(4):453-62. doi: 10.1176/appi.ajp.2013.13030325
24. Colman I, Kingsbury M, Sucha E, Horton NJ, Murphy JM, Gilman SE. Depressive and anxious symptoms and 20-year mortality: Evidence from the Stirling County study. *Depress Anxiety*. 2018 Jul;35(7):638-647. doi: 10.1002/da.22750
25. Das-Munshi J, Chang CK, Schofield P, Stewart R, Prince MJ. Depression and cause-specific mortality in an ethnically diverse cohort from the UK: 8-year prospective study. *Psychol Med*. 2019;49(10):1639-1651. doi:10.1017/S0033291718002210, 10.1017/S0033291718002210
26. Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Is excess mortality higher in depressed men than in depressed women? A meta-analytic comparison. *J Affect Disord*. 2014 Jun;161:47-54. doi: 10.1016/j.jad.2014.03.003
27. Gilman SE, Sucha E, Kingsbury M, Horton NJ, Murphy JM, Colman I. Depression and mortality in a longitudinal study: 1952-2011. *CMAJ*. 2017 Oct 23;189(42):E1304-E1310. doi: 10.1503/cmaj.170125
28. Høye A, Nesvåg R, Reichborn-Kjennerud T, Jacobsen BK. Sex differences in mortality among patients admitted with affective disorders in North Norway: a 33-year prospective register study. *Bipolar Disord*. 2016 May;18(3):272-81. doi: 10.1111/bdi.12389
29. Mykletun A, Bjerkeset O, Overland S, Prince M, Dewey M, Stewart R. Levels of anxiety and depression as predictors of mortality: the HUNT study. *Br J Psychiatry*. 2009 Aug;195(2):118-25. doi: 10.1192/bjp.bp.108.054866
30. Zivin K, Yosef M, Miller EM, et al. Associations between depression and all-cause and cause-specific risk of death: a retrospective cohort study in the Veterans Health Administration. *J Psychosom Res*. 2015;78(4):324-31. doi:10.1016/j.jpsychores.2015.01.014, 10.1016/j.jpsychores.2015.01.014
31. Foley DL, Goldston DB, Costello EJ, Angold A. Proximal psychiatric risk factors for suicidality in youth: the Great Smoky Mountains Study. *Arch Gen Psychiatry*. 2006 Sep;63(9):1017-24. doi: 10.1001/archpsyc.63.9.1017
32. Statistics Finland. Suomen virallinen tilasto (SVT): Kuolemansyyt. [Internet]. 2021 [referenced at 3.2.2022]. Available: <http://www.stat.fi/til/ksyyt/index.html>
33. Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *Br J Psychiatry*. 1997 Mar;170:205-28. doi: 10.1192/bjp.170.3.205
34. Hintikka U, Marttunen M, Pelkonen M, Laukkanen E, Viinamäki H, Lehtonen J. Improvement in cognitive and psychosocial functioning and self-image among adolescent inpatient suicide attempters. *BMC Psychiatry*. 2006 Dec 29;6:58. doi: 10.1186/1471-244X-6-58
35. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The Global Assessment Scale. A procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976 Jun;33(6):766-71. doi: 10.1001/archpsyc.1976.01770060086012
36. Richter D, Berger K, Reker T. Nehmen psychische Störungen zu? Eine systematische Literaturübersicht [Are mental disorders on the increase? A systematic review]. *Psychiatr Prax*. 2008 Oct;35(7):321-30. German. doi: 10.1055/s-2008-1067570

37. Costello EJ, Erkanli A, Angold A. Is there an epidemic of child or adolescent depression? *J Child Psychol Psychiatry*. 2006 Dec;47(12):1263-71. doi: 10.1111/j.1469-7610.2006.01682.x
38. Sourander A, Koskelainen M, Niemelä S, Rihko M, Ristkari T, Lindroos J. Changes in adolescents' mental health and use of alcohol and tobacco: a 10-year time-trend study of Finnish adolescents. *Eur Child Adolesc Psychiatry*. 2012 Dec;21(12):665-71. doi: 10.1007/s00787-012-0303-8
39. Mishina K, Tiiri E, Lempinen L, Sillanmäki L, Kronström K, Sourander A. Time trends of Finnish adolescents' mental health and use of alcohol and cigarettes from 1998 to 2014. *Eur Child Adolesc Psychiatry*. 2018 Dec;27(12):1633-1643. doi: 10.1007/s00787-018-1158-4
40. Gyllenberg D, Bastola K, Wan Mohd Yunus WMA, Mishina K, Liukko E, Kääriälä A, Sourander A. Comparison of new psychiatric diagnoses among Finnish children and adolescents before and during the COVID-19 pandemic: A nationwide register-based study. *PLoS Med*. 2023 Feb 27;20(2):e1004072. doi: 10.1371/journal.pmed.1004072
41. Horwitz AV. How an age of anxiety became an age of depression. *Milbank Q*. 2010 Mar;88(1):112-38. doi: 10.1111/j.1468-0009.2010.00591.x
42. Statistics Finland. 7. Itsemurhia aiempaa vähemmän. [Internet]. 2020 [referenced at 5.8.2023]. Available: http://www.stat.fi/til/ksyyt/2020/ksyyt_2020_2021-12-10_kat_007_fi.html
43. Statistics Finland. Terveys > Elinajanodote. [Internet]. 2021 [referenced at 18.2.2023]. Available: <https://www.tilastokeskus.fi/tup/tasaarvo/terveys>
44. Ohannessian CM, Fagle T, Salafia C. Social media use and internalizing symptoms during early adolescence: The role of co-rumination. *J Affect Disord*. 2021 Feb 1;280(Pt A):85-88. doi: 10.1016/j.jad.2020.10.079
45. Rosa H. Social acceleration: ethical and political consequences of a desynchronized high-speed society. *Constellations*. 2003 Mar;10(1):3-33. doi: 10-1111/1467-8675.00309
46. Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. *Scand J Public Health*. 2012 Aug;40(6):505-15. doi: 10.1177/1403494812456637



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ADOLESCENT INPATIENTS WITH A DEPRESSIVE DISORDER: TREATMENT OUTCOMES AND PSYCHOPHARMACOLOGICAL MEDICATION

ABSTRACT

This study examined the efficacy of psychiatric inpatient treatment and the use of psychopharmacological medication in adolescents with a depressive disorder. The study sample consisted of 13–17 years old adolescents (n=256) treated due to a depressive disorder in the two adolescent psychiatric units of Kuopio University Hospital, Finland, during the ten years 2002–2011. The data concerning demographic and clinical characteristics, treatment outcomes and medication were collected from the patients' medical records. Approximately 70% of hospitalizations terminated with satisfactory clinical results. Inpatient treatment was more beneficial for the patients with a non-psychotic depression, whereas every second adolescent with a psychotic depression had still low psychosocial functioning at discharge (median GAS scores at discharge 45 vs. 40, $p=0.001$). Psychotropic medication was utilized in 95% of all hospitalizations. Mirtazapine, selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics were the most frequently prescribed medications. Antidepressants and antipsychotics induced adverse events rather frequently (23% and 31%, respectively), but serious side effects such as worsening of psychiatric symptoms, cardiac problems and metabolic changes were rare. Psychopharmacological medication has to be individually tailored and require frequent monitoring of the clinical response, side effects and safety. Both clinical and controlled trials investigating the utility of psychopharmacological treatments in young patients are needed.

KEYWORDS: ADOLESCENT, DEPRESSIVE DISORDER, PSYCHIATRIC INPATIENT TREATMENT, TREATMENT OUTCOME, PSYCHOPHARMACOLOGICAL MEDICATION

INTRODUCTION

Depression is a common and serious psychiatric disorder in adolescents; the 12-month prevalence has been estimated to be 7.5% among US and 10.5% among European adolescents, but many more young persons, almost three out of every ten (29.2%) are estimated to have a subthreshold depression [1,2]. The lifetime prevalence of psychotic depression is estimated to be 0.5% [3]. The prevalence of depression is higher among girls, and it increases as adolescence proceeds [2].

Depression may have many long-term effects on the course of an individual's life, such as severe role impairment, problems at school and difficulties with social relationships [2,4]. Depressed adolescents have a higher risk for substance misuse, self-harm and suicidal behaviour. Furthermore, the occurrence of comorbid mental disorders, especially anxiety and behavioural disorders, is common. It is evident that the efficacious treatment of depression would not only reduce costs to society, but would also increase the quality of life of the adolescent and improve his/her mental health in the transition to adulthood.

Most depressive disorders in adolescents are treated in outpatient care, but hospitalization is needed if there is a high risk of serious self-harm, suicidality, self-neglect or severe impairment in psychosocial functioning. The principal treatment of depression in these young people consists of various therapeutic interventions [5,6]. First-line treatment of adolescents with mild or moderate depression is not antidepressant medication, but psychopharmacological intervention is needed in cases of severe and psychotic depression.

Psychopharmacological medication is often used “off-label” in underage patients, i.e., without an official indication. According to the database of the Social Insurance Institution of Finland, the number of prescriptions for antidepressants for young people has increased significantly in recent decades, with the same trend also being observed in other countries [7-10]. The prescribing of psychotropic medication to adolescents in hospital settings became more common in the 1990s; in 1991 only 29% of depressive adolescent inpatients were medicated, by 1999 that percentage had risen to 71% [11].

Although there are many antidepressants on the market, fluoxetine is the only compound that has shown therapeutic efficacy in clinical trials in the treatment of depression of teenage individuals [12] and the guidelines recommend it as the first-line antidepressant [5,6]. It is essential that patients must be monitored carefully at the start of therapy because

adverse events, even suicidal behaviour, are possible. If fluoxetine is inefficient or induces side effects, sertraline, citalopram and escitalopram are recommended. After remission, antidepressant medication should be continued for at least six months to prevent relapse.

The aims of this study were to examine the efficiency of the psychiatric inpatient treatment of adolescents suffering from depressive disorders and the use of psychopharmacological medication utilized during hospitalizations.

METHODS

SAMPLE

The study sample consisted of 13–17 years old adolescents (n=256, 87% females) treated due a depressive disorder in the two adolescent psychiatric units of Kuopio University Hospital, Finland, during the years 2002–2011. These units serve as a tertiary care centre for a catchment area of North Savo District, which has around one million inhabitants. Both voluntary and involuntary forms of treatment were provided. The treatment was individualized and consisted of therapeutic sessions with a case manager nurse at least once a week, along with different activities, family sessions, and somatic consultation and psychopharmacological medication when appropriate [13].

The criteria for inclusion in the study were a duration of hospitalization of at least five days and that data collected via the Beck Depression Inventory questionnaire (BDI) was available at both admission and discharge. Patients with a bipolar disorder or dysthymia were excluded from this study. In addition, patients with a depressive conduct disorder were excluded from the study because the results relating to these individuals have been published earlier [14]. Patients with cyclothymia were included.

Data collection and assessment methods

The diagnosis of depression was made by a psychiatric interview according to ICD-10 (International Classification of Diseases, version 10) criteria as part of the clinical examination performed by a psychiatrist specializing in adolescent care. The patients' diagnoses at discharge were categorized into three groups according to the severity of depression diagnosis as follows: 1) mild/moderate depression or cyclothymia (F32.0, F32.1, F33.1, F34.0), 2) severe depression without psychotic symptoms (F32.2, F33.2) and 3) severe depression with psychotic symptoms (F32.3, F33.3) (*Table 1*). The clinical results are presented for these diagnostic groups.

Table 1. Characteristics of the psychiatric inpatient treatment periods of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms	p-value
Treatment periods, n	85	183	81	
The first psychiatric hospitalization, n (%)	54 (64%)	113 (62%)	27 (33%)	< 0.001 ($\chi^2(2)=21.234$)
Involuntary treatment, n (%)	11 (13%)	29 (16%)	29 (36%)	< 0.001 ($\chi^2(2)=17.400$)
The length of hospitalization (days), median (range)	13 (5 – 86)	22 (5 – 96)	25 (5 – 369)	< 0.001

Demographic and clinical characteristic data including estimations of depressive symptoms (Beck Depression Inventory, BDI), hopelessness (Beck’s Hopelessness Scale, HS) and psychosocial functioning (Global Assessment Scale, GAS) were collected from the patients’ medical records.

BDI is a numeric self-rated scale used to measure the severity of depression in a subjective manner [15]. The scores range from zero to sixty-three; higher scores represent more severe depressive symptoms. Scores less than 13 indicate minimal depression, scores from 13 to 18 point to mild depression, scores from 19 to 29 refer to moderate depression and scores from 30 to 63 are evidence of severe depression.

HS is a numeric self-rated scale used to measure subjectively feelings of pessimism and hopelessness [16]. Its scores range from 0 to 20; values under nine refer to mild or insignificant hopelessness whereas scores of fifteen or more represent critical hopelessness.

GAS is a numeric scale used to assess an individual’s psychosocial functioning [17]. GAS scores were evaluated by the hospital staff team. The scores range from one to a hundred with the scale being divided into ten equal intervals. Low scores indicate poor psychosocial functioning with the upper value of a hundred representing superior functioning. Constant monitoring is needed when an individual’s scores are less than ten, scores less than 41 refer to severe psychosocial functional impairment in several areas whereas scores of seventy or more are regarded as a good functional capability.

In addition to BDI, HS and GAS scores, the data assessing the efficacy of psychiatric hospitalizations were collected from

the medical case summaries. The outcome of treatment was assessed as a dichotomous variable (satisfactory/non-satisfactory) and it was based on the estimation by the staff team. The data concerning psychotropic drug therapy including antidepressants, antipsychotics and anxiolytics as well as sedatives and other psychopharmacological medication, such as mood stabilizers, methylphenidate and naltrexone, were collected from the medical records.

STATISTICAL ANALYSES

The data were analysed using IBM SPSS Statistics 27 Software. Continuous variables were categorized as means or medians, and categorical variables as percentages. The statistical significance for categorical variables was analysed using Chi-squared test. For numeric variables of independent samples, Mann-Whitney U test was used to compare two groups and Kruskal-Wallis test to compare more than two groups. P values below 0.05 were used to indicate a statistically significant difference.

ETHICAL CONSIDERATIONS

The permission for this study was provided by the Research Ethics Committee of the Northern Savo Hospital District (the approval number 272/2016) and University of Eastern Finland and by the Medical Director of the University Hospital of Kuopio. Notification of the research was also delivered in advance of data collection to the Data Protection Ombudsman.

RESULTS

PATIENT CHARACTERISTICS

During the ten-year study period (2002–2011), there were 349 inpatient treatment periods (*Table 1*). Each patient had on average 1.4 (range of 1–9) hospitalizations during the study period. Over 60% of treatment periods with a diagnosis of cyclothymia or mild, moderate or severe depression without psychotic symptoms represented an individual’s first psychiatric hospitalization, whereas two out of every three patients with psychotic symptoms had been previously hospitalized for psychiatric symptoms. The median length of hospital treatment was 20 days (range 5–369 days). The longest treatment periods were observed in those patients with psychotic depression.

Most of the adolescents were females (*Table 2*). Self-destructive thoughts and/or behaviour, sleep problems and anxiety were common symptoms. A suicide attempt preceded every fifth hospitalization. Every fifth adolescent exhibited a comorbid psychiatric disorder. Neurotic, stress-related and somatoform disorders (6%), as well as eating disorders (5%) were the two most common comorbid psychiatric diagnoses. The first of these disorders was particularly evident in the patients diagnosed with either mild/moderate depression or cyclothymia with the latter comorbidity being more common in the adolescents suffering from severe depression without psychotic symptoms.

Table 2. Demographic and clinical characteristics of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms	p-value
Age at admission, mean (range)	16.2 (13.6 – 17.9)	15.9 (13.3 – 17.9)	16.2 (13.6 – 17.9)	ns
Female, n (%)	76 (89%)	159 (87%)	75 (93%)	ns
Fostered, n (%)	16 (19%)	32 (17%)	17 (21%)	ns
Suicide attempts, n (%)	13 (15%)	47 (26%)	18 (22%)	ns
Self-destructive thoughts and/or behaviour, n (%)	76 (89%)	163 (89%)	78 (96%)	ns
Sleep disturbances, n (%)	56 (66%)	139 (76%)	50 (62%)	0.04 ($\chi^2(2)=6.435$)
Anxiety symptoms, n (%)	53 (62%)	126 (69%)	68 (84%)	0.007 ($\chi^2(2)=10.040$)

ns = not significant

TREATMENT OF PATIENTS WITH MILD OR MODERATE DEPRESSION OR CYCLOTHYMIA

At the end of hospital treatment, the outcome of treatment was estimated by the staff team. Most hospitalizations (78%) of the patients with mild or moderate depression or cyclothymia ended with satisfactory clinical results. In line with this, psychosocial functioning was still low (GAS <41)

in 19% of patients at discharge (Table 3). Positive changes were observed in all psychiatric assessments (BDI, HS, GAS). However, almost every second inpatient treatment (48%) was followed by a psychiatric hospitalization during the ten-year study period.

Table 3. BDI, GAS and HS scores of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms
Severe depression			
BDI ≥ 30 at admission, n (%)	26 (31%)	106 (58%)	48 (59%)
BDI ≥ 30 at discharge, n (%)	6 (7%)	51 (28%)	17 (21%)
Moderate depression			
BDI = 19–29 at admission, n (%)	39 (46%)	48 (26%)	21 (26%)
BDI = 19–29 at discharge, n (%)	13 (15%)	36 (20%)	27 (33%)
Mild depression			
BDI = 13–18 at admission, n (%)	12 (14%)	13 (7%)	5 (6%)
BDI = 13–18 at discharge, n (%)	20 (24%)	26 (14%)	13 (16%)
Minimal depression			
BDI < 13 at admission, n (%)	8 (9%)	16 (9%)	7 (9%)
BDI < 13 at discharge, n (%)	46 (54%)	70 (38%)	24 (30%)
Critical hopelessness			
HS ≥ 15 at admission, n (%)	14 (25%) ^a	58 (50%) ^b	27 (42%) ^c
HS ≥ 15 at discharge, n (%)	6 (11%) ^a	28 (24%) ^b	17 (26%) ^c
Severe psychosocial functional impairment			
GAS < 41 at admission, n (%)	59 (92%) ^d	101 (92%) ^e	58 (100%) ^f
GAS < 41 at discharge, n (%)	12 (19%) ^d	24 (22%) ^e	31 (53%) ^f

Abbreviations: BDI = Beck Depression Inventory, HS = Beck’s Hopelessness Scale, GAS = Global Assessment Scale

^a data missing from 28 treatment periods
^b data missing from 67 treatment periods
^c data missing from 16 treatment periods
^d data missing from 21 treatment periods
^e data missing from 73 treatment periods
^f data missing from 23 treatment periods

Psychotropic medication was administered to most patients (Table 4). Over half of the antidepressants (60%) and antipsychotics (53%) had been initiated during outpatient care. While mirtazapine and selective serotonin reuptake inhibitors (SSRIs) were the most often prescribed antidepressants, venlafaxine, duloxetine and agomelatine were also administered in a few cases. Every fourth adolescent was treated with antidepressants together with an antipsychotic

medication. These combinations were more rarely used during the first hospitalization as compared to subsequent ones (13% vs. 42%). Antidepressants evoked adverse events rather frequently (in 21% of medications) (Table 5). In fact, psychiatric symptoms that demanded a discontinuation of antidepressant medication occurred only in three patients. In addition, a course of citalopram therapy was discontinued once due to tachycardia.

Table 4. The most frequently prescribed psychotropic medications in the hospitalization of adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia		Severe depression without psychotic symptoms		Severe depression with psychotic symptoms	
	n	%	n	%	n	%
Psychotropic medication	73	86	177	97	81	100
Antidepressant	53	62	156	85	46	57
Mirtazapine	24	28	88	48	15	19
Escitalopram	12	14	53	29	20	25
Fluoxetine	11	13	48	26	8	10
Citalopram	7	8	13	7	3	4
Antipsychotic	36	42	91	50	77	95
Quetiapine	28	33	74	40	40	49
Olanzapine	6	7	9	5	36	44
Clozapine	0	0	4	2	24	30
Aripiprazole	1	1	4	2	19	23
Antidepressant + antipsychotic	20	24	72	39	42	52
Anxiolytic	21	25	62	34	50	62
Oxazepam	19	22	55	30	39	48
Sedative	37	44	72	39	37	46
Zopiclone	26	31	55	30	22	27

Table 5. The adverse events of antidepressant treatment of adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

Adverse event	Mirtazapine (n=127)	Escitalopram (n=85)	Fluoxetine (n=67)	Citalopram (n=23)	Venlafaxine (n=21)	Sertraline (n=9)	Duloxetine (n=6)
Psychiatric							
- provoked psychiatric symptoms (n)	4	13	3	2	1	1	0
- sleep disorder (n)	2	2	0	0	0	0	1
Nervous system							
- fatigue (n)	15	3	2	1	0	1	0
- headache (n)	0	4	0	0	1	0	0
- dizziness (n)	4	0	1	0	1	0	0
- drowsiness (n)	3	0	0	0	0	0	0
- tremor (n)	1	1	0	0	0	0	0
- convulsion (n)	1	0	0	0	0	0	0
Cardiac							
- tachycardia (n)	0	1	0	1	0	0	0
Vascular							
- low blood pressure / fainting (n)	0	0	0	0	1	0	0
Autonomic							
- dry mouth (n)	1	1	0	0	0	0	0
Gastrointestinal							
- nausea (n)	1	2	3	1	1	1	1
- abdominal pain (n)	0	0	1	0	0	0	0
Metabolism and nutrition							
- increased appetite (n)	4	0	1	0	0	0	0
- weight gain (n)	2	0	1	0	0	0	0
Respiratory							
- breathing difficulty (n)	1	0	0	0	0	0	0
Skin and subcutaneous tissue							
- exanthema (n)	1	0	0	0	0	0	0
- sweating (n)	0	0	1	0	0	0	0
Musculoskeletal							
- arthralgia (n)	1	0	0	0	0	0	0
Eye							
- mydriasis (n)	0	2	0	0	0	0	0
Reproductive system							
- sexual adverse events (n)	0	0	0	1	0	0	0
Hepatobiliary							
- elevated liver enzymes (n)	0	1	1	0	0	0	0

Antipsychotics were utilized in nearly half of the hospitalizations; quetiapine and other atypical antipsychotics were prescribed more commonly (Table 4). The average daily doses of quetiapine and olanzapine were 197mg and 9mg, respectively. Quetiapine was occasionally used for off-label indications as a sedative and/or as an anxiolytic (according to 25% of the prescriptions) and the average daily dose in these indications was 58mg. One olanzapine medication was administered due to its sedative and anxiolytic properties. In addition, lithium was prescribed in a few cases (n=3). Every fourth antipsychotic medication (27%) resulted in adverse effects (Table 6). However, only one patient experienced such severe quetiapine-induced fatigue and restless legs that this medication had to be terminated.

Table 6. The adverse events of antipsychotic treatments most used by adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

Adverse event	Queti- apine (n=142)	Olan- zapine (n=51)	Clozapine (n=28)	Aripip- razole (n=24)	Chlorpro- thixene (n=13)	Risper- idone (n=11)
Psychiatric						
- provoked psychiatric symptoms (n)	5	1	1	1	0	0
- sleep disorder (n)	2	1	0	0	0	0
Nervous system						
- fatigue (n)	27	5	8	0	0	0
- headache (n)	3	1	0	2	0	0
- dizziness (n)	7	0	3	2	0	0
- drowsiness (n)	2	0	0	0	1	0
- tremor (n)	0	2	2	0	0	0
- restless legs (n)	2	0	0	0	0	0
- motor difficulties (n)	1	0	0	0	0	0
- oculogyric crisis (n)	1	0	0	0	0	0
- stiffness (n)	0	1	0	0	0	0
Cardiac						
- tachycardia (n)	2	0	1	0	0	0
- arrhythmia (n)	3	0	0	0	0	0
- QTc prolongation (n)	0	1	0	0	0	0
Vascular						
- low blood pressure / fainting (n)	1	0	1	0	0	0
Autonomic						
- dry mouth (n)	3	1	0	0	0	0



Adverse event	Queti- apine (n=142)	Olan- zapine (n=51)	Clozapine (n=28)	Aripip- razole (n=24)	Chlorpro- thixene (n=13)	Risper- idone (n=11)
Gastrointestinal						
- nausea (n)	1	0	3	2	0	0
- heartburn (n)	2	0	0	0	0	0
- constipation (n)	1	0	1	0	0	0
- hypersalivation (n)	0	0	13	0	0	0
Metabolism and nutrition						
- increased appetite (n)	1	3	0	0	0	0
- weight gain (n)	3	6	5	0	0	0
- hyperlipidemia (n)	0	1	0	0	0	0
Respiratory						
- breathing difficulty (n)	3	0	1	0	0	0
Skin and subcutaneous tissue						
- exanthema (n)	1	0	0	0	0	0
- oedema (n)	1	0	0	0	0	0
Eye						
- dry eyes (n)	1	0	0	0	0	0
Reproductive system						
- galactorrhoea (n)	0	1	0	0	0	1
- hormonal imbalance (n)	0	1	0	0	0	0
Renal and urinary						
- dysuria (n)	1	0	2	0	0	0

Oxazepam was the most often prescribed anxiolytic drug and zopiclone was the most common sedative (*Table 4*). In two patients, the anxiolytic medication had to be discontinued due to adverse effects: oxazepam due to confusion and chlordiazepoxide due to neck twinges. Sedatives induced adverse effects very rarely. In addition, lamotrigine was administered to a single patient.

TREATMENT OF PATIENTS WITH SEVERE DEPRESSION WITHOUT PSYCHOTIC SYMPTOMS

Over half of hospitalizations (66%) of the patients with severe depression without psychotic symptoms ended with satisfactory clinical results. Although there were positive changes in psychiatric assessments, psychosocial functioning was low (GAS <41) at discharge in every fifth patient (22%) (*Table 3*). Patients also returned to psychiatric hospital treatment rather often; after 53% of inpatient treatments.

Almost all, 97% of patients, received psychopharmacological medication (*Table 4*). Slightly over half of antidepressants (52%) and antipsychotics (51%) had been initiated during outpatient care. Mirtazapine and SSRIs were the most frequently prescribed antidepressants, but venlafaxine, duloxetine and agomelatine were administered to some patients. Antidepressants were combined with antipsychotics in 39% of the hospitalizations. The patients who were treated with these combinations had higher average BDI depression scores (33 vs. 29, $p=0.042$) and HS scores (15 vs. 12, $p=0.008$) at admission than the other adolescents. In addition, the length of their hospitalizations was also longer (median 24 days vs. 14 days, $p=0.043$). Antidepressant therapy was often associated with adverse events (in 22% of medications); for example, a worsening of psychiatric symptoms led to the termination of the drug therapy in four patients (*Table 5*).

Antipsychotics were used in every second psychiatric inpatient treatment (*Table 4*) with quetiapine and other atypical antipsychotics being most often prescribed. The average daily doses of quetiapine and olanzapine were 175mg and 10mg, respectively. Quetiapine was administered mostly due to its antipsychotic, antidepressant and mood stabilizing properties. However, in 34% of the prescriptions, it was used as a sedative and/or as an anxiolytic (an average daily dose 81mg). Chlorprothixene (regular use n=1, irregular use n=5), lithium (n=1) and irregularly used levomepromazine (n=1) were also prescribed to some adolescents. Every fourth antipsychotic medication (26%) resulted in adverse effects (*Table 6*). A major increase in the body weight of one patient led to the discontinuation of olanzapine medication and quetiapine-induced fatigue and drowsiness were reasons to terminate this medication in two individuals.

Anxiolytics and sedatives were prescribed in 34% and 39% of the treatment periods, respectively (*Table 4*). Oxazepam and zopiclone were the most commonly used medicines from these two drug groups. Anxiolytics and sedatives caused adverse effects very rarely. Oxazepam triggered symptoms of fatigue in one patient and zopiclone caused hallucinations and/or an unpleasant taste in two patients; for these reasons, the medications were discontinued. Other psychotropic medications (lamotrigine n=3, methylphenidate n=1 and topiramate n=1) were rarely needed.

TREATMENT OF PATIENTS WITH SEVERE DEPRESSION WITH PSYCHOTIC SYMPTOMS

Although over half of the hospitalizations (58%) of the patients with severe depression with psychotic symptoms ended with satisfactory clinical results, 53% of these adolescents had severely impaired psychosocial functioning (GAS <41) at discharge (*Table 3*). Therefore, it was not surprising that adolescents from this patient group often returned to inpatient care (after 83% of inpatient treatments) during the ten-year study period.

All patients received psychotropic medication during their inpatient treatment (*Table 4*). In fact, most of them had started antidepressant and antipsychotic medications already during their outpatient care, 65% and 73%, respectively. SSRIs and mirtazapine were the most generally prescribed antidepressants, but venlafaxine, duloxetine and agomelatine were also occasionally administered. Antidepressants were often combined with antipsychotics. Antidepressant-induced adverse events were observed in 28% of medications (*Table*

5). For example, a worsening of psychiatric symptoms led to discontinuation of antidepressants in three patients.

Antipsychotics were prescribed to 95% of these patients (*Table 4*). Atypical antipsychotics were utilized most frequently, but other drugs such as chlorprothixene (regular use n=1, irregular use n=6), lithium (n=2), irregularly used haloperidol (n=2) and regularly used levomepromazine (n=1) were administered to some patients. Quetiapine and olanzapine were used occasionally as sedatives and/or as anxiolytics (10% of quetiapine and 14% of olanzapine) and the average daily doses in these indications were 81mg and 14mg, respectively. In this patient group, higher doses of quetiapine, olanzapine and clozapine were needed (the average daily doses 326mg, 15mg, 346mg, respectively) as compared to the other patients in this study (in them, the average daily doses were 181mg, 10mg, 113mg, respectively). The average daily doses of aripiprazole and chlorprothixene were 12mg and 100mg, respectively.

Antipsychotics caused adverse effects rather often (in 35% of medications) (*Table 6*). Quetiapine and clozapine caused such severe weight gains that it led to a discontinuation of the medications in two patients. Quetiapine also induced cardiac problems in one patient and fatigue in another one, both being reasons to cease drug treatment. Olanzapine and risperidone triggered hormonal disturbances in two patients leading to a discontinuation of these medications.

Anxiolytics and sedatives were often utilized (*Table 4*). These drugs evoked rather few adverse effects, but drowsiness caused by lorazepam was a reason to stop this medication in one patient. Other psychotropic medications (lamotrigine n=3, valproic acid n=2 and naltrexone n=1) were administered only occasionally.

DISCUSSION

This clinical study examined the efficacy of psychiatric hospital treatment and the use of psychopharmacological medication in adolescents suffering from a depressive disorder. The treatment of depressed adolescents needing inpatient psychiatric treatment is demanding; it should be conducted by a multi-professional team and often psychopharmacological treatment is also required. According to the assessments of the treatment teams, two-thirds of hospitalizations ended with satisfactory clinical results. Although there are only a few medicines with an official indication for young patients, psychopharmacological treatment was commonly used

with mirtazapine, SSRIs and atypical antipsychotics being the most frequently prescribed medications. Serious side effects of psychotropic medication, such as worsening of psychiatric symptoms, cardiac problems and metabolic changes, was rare.

According to the changes of BDI, HS and GAS scores, patients' symptoms of depression and feelings of hopelessness were relieved and their functional capacity improved significantly during the hospital stay. Inpatient treatments were particularly successful for those patients without psychotic depression. These adolescents were mainly in voluntary treatment and many of them were in the psychiatric ward for the first time, which might partly explain the good treatment outcome. Most hospitalizations (70%) of the patients in these diagnostic groups ended with satisfactory clinical results, but still every second adolescent returned to psychiatric inpatient care during the study period. Although there is a trend for short stays in psychiatric wards, some researchers have linked a short length of stay to increased rates of rehospitalization [18]. If patients are discharged with residual symptoms and clinical problems (e.g., psychosocial issues have not been addressed), this may diminish their potential to experience a sustained recovery. It has also been reported that an older age and lower GAS scores at admission are factors affecting the improvement of children and adolescents treated in psychiatric inpatient units [19,20]. Though most of the adolescents with a mild or moderate depression or cyclothymia can be treated in outpatient care, hospitalizations may have been needed, e.g., due to a comorbid psychiatric disorder, suicidality or inadequate outpatient care.

The treatment outcomes of adolescents with severe psychotic depression were less impressive. Over half of hospitalizations ended with satisfactory clinical results, but still every second adolescent had severely impaired psychosocial functioning at discharge although they had longer inpatient treatment periods compared to the patients without psychotic depression. In addition, these patients required hospitalization again after 83% of the initial treatment periods. This result highlights the seriousness of this disorder. However, the inpatient treatment seems to be more beneficial for the adolescents with depression compared to the young patients with a depressive conduct disorder because only 25.5% of the hospitalizations ended with satisfactory clinical results in the latter group [14]. In conclusion, psychiatric inpatient care seems to be effective for the majority of young people though research in adolescent inpatient settings is rather limited [18-21].

Psychotropic medication was prescribed to almost all adolescents during their hospital stay. Antidepressants were commonly used, although their efficacy has not been unequivocally demonstrated [22]. According to the recent meta-analysis of Hetrick et al. [23], most of the newer generation antidepressants reduce depression symptoms to some extent. In this study, mirtazapine was the most widely prescribed antidepressant although fluoxetine has been demonstrated to possess therapeutic efficacy [12,22] and it is recommended as the first-line antidepressant for patients under 18 years of age [5,6]. The popularity of mirtazapine can be partly explained by its sedative and anxiolytic effects [24]. Most adolescents in this study had been treated as outpatients and many of them also as inpatients, and therefore it is possible that fluoxetine may have been prescribed previously for some of them. According to Finnish guidelines, sertraline and escitalopram are recommended as second-line treatments if fluoxetine is not suitable either due to side effects or poor efficacy [5]. Other SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) such as duloxetine can also be considered [5,23].

While paroxetine seems to lack efficacy in adolescents [25,26], it may reduce depressive symptoms at least to a minor extent in older teenagers [27]. Venlafaxine may be efficient in adolescent depression, but it may carry a risk for suicidality [23,28]. It appears that both paroxetine and venlafaxine induce more adverse events than placebo [25-28], and they are unsuitable for the treatment of juvenile depression [6]. Tricyclic antidepressants may reduce only slightly the symptoms of depression in adolescents [4], but they are not recommended because of their marginal efficacy, adverse events and potential toxicity [5,6]. The administration of these medications seemed to be in line with the guidelines and scientific literature because paroxetine and venlafaxine had been prescribed rarely and tricyclic antidepressants not at all.

Antipsychotic medications were surprisingly commonly administered to young patients, since 42-95% of adolescents in the different diagnostic groups received these pharmaceuticals. Quetiapine was the most common antipsychotic, and while it was most often utilized for its antipsychotic effects, it was also prescribed due to its anxiolytic and/or sedative properties [29]. Antidepressants were combined with antipsychotics particularly in the treatment of psychotic depression.

In this study, antidepressants and antipsychotics induced adverse events rather frequently, but serious side effects were rare. Antidepressants were discontinued due to worsening of psychiatric symptoms in ten adolescents. Antipsychotics were

discontinued mainly due to fatigue and severe weight gain. Clozapine caused most often adverse events and it should never be considered as the first-choice drug [30]. Here, it was prescribed to the adolescents with psychotic depression and infrequently to some patients with severe depression without psychotic symptoms. However, all patients receiving clozapine had been hospitalized due to a psychotic depression at least once during the study period.

Sleeping difficulties and anxiety are commonly encountered when treating patients with depression, and insomnia seems to be a rather ubiquitous symptom in depressed adolescents as compared to adults [31]. These symptoms were reported in 70% of treatment periods, but sedatives and anxiolytics were prescribed only in 42% and 40% of hospitalizations, respectively. Sedatives and anxiolytics may have been avoided possibly due to their risk for addiction; this might partly explain the rather high usage rates of antipsychotics in the patients with cyclothymia and depression without psychotic symptoms. Antipsychotics should be prescribed to patients with sleeping difficulties only in special cases [32]. In the case of young patients, melatonin could reduce sleep latency, but non-drug-based approaches should represent the first-line treatment.

In conclusion, the treatment of adolescents with a depressive disorder consists of various psychosocial interventions and psychopharmacological agents. Overall, the psychotropic medication of the hospitalized adolescents seemed to be in accordance with the guidelines. The main principles of the treatment have remained the same in the last decades and psychotropic medications have been studied for a long time. However, there is not a one-size-fits-all treatment of young patients with a depressive disorder. Therefore, psychotropic medication should be tailored individually, and possible adverse events, such as psychiatric, metabolic, extrapyramidal, cardiovascular and hormonal effects, must be considered and monitored carefully throughout the course of the treatment. It is evident that both clinical and controlled trials clarifying the utility of these medications would be beneficial.

STRENGTHS AND LIMITATIONS

The present study has some limitations. It was a retrospective study examining psychopharmacological medication used during the inpatient treatment of depressed adolescents. The data were collected from patients' medical records which had not been written for scientific purposes. Because of

missing data of GAS and HS scores, the results concerning the functional capacity and pessimistic attitude may not be totally reliable. However, this method may obtain more authentic results than possible with other approaches such as interviews.

BDI and HS are validated, reliable and globally used measures. It is noteworthy that BDI and HS are self-assessment scales, and it is possible that some patients were not capable of recognizing their own feelings or suicidal ideation. In contrast, the GAS assessments were made by the staff team. The use of these standardized and reliable scales strengthens the results of the study.

While diagnoses were made by psychiatrists using the ICD-10 diagnostic system, structured interviews might have been more reliable. A wider perspective of the depressed adolescents' treatment would have been acquired if we had had access to the data from outpatient care. It could be argued that intensive and effective outpatient care could prevent psychiatric hospitalization. Inadequacy or even a total lack of appropriate outpatient care and feelings of hopelessness can lead to the patient's symptoms deteriorating to the extent that he/she requires psychiatric inpatient treatment.

Inpatient treatment of depressed adolescents is rather rare, because the majority of the patients can be treated as outpatients. Thus, the results provide a perspective of the outcomes of inpatient treatment and the use of psychotropic drugs in everyday practice in a clinical ward treating depressed adolescents.

Disclosures

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References

1. Balázs J, Miklósi M, Keresztény A et al. Adolescent subthreshold-depression and anxiety: psychopathology, functional impairment and increased suicide risk. *J Child Psychol Psychiatry*. 2013;54(6):670–677.
2. Avenevoli S, Swendsen J, He J et al. Major depression in the national comorbidity survey-adolescent supplement: prevalence, correlates, and treatment. *J Am Acad Child Adolesc Psychiatry*. 2015;54(1):37–44.
3. Nietola M, Huovinen H, Heiskala A et al. Early childhood and adolescent risk factors for psychotic depression in a general population birth cohort sample. *Soc Psychiatry Psychiatr Epidemiol*. 2020;55(9):1179–1186.
4. Hazell P, Mirzaie M. Tricyclic drugs for depression in children and adolescents. *Cochrane Database Syst Rev*. 2013;2013(6):CD002317. DOI: 10.1002/14651858.CD002317.pub2.
5. Depression. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Psychiatric Association. Helsinki: The Finnish Medical Society Duodecim. 2023 (cited 2023 Apr 14). Available from: www.kaypahoito.fi
6. National Institute for Health and Care Excellence (NICE). Depression in children and young people: Identification and management. Nice Guideline 134. 2019 [cited 2022 Dec 20]. Available from: <https://www.nice.org.uk/guidance/ng134>
7. John A, Marchant AL, Fone DL et al. Recent trends in primary-care antidepressant prescribing to children and young people: an e-cohort study. *Psychol Med*. 2016;46(16):3315–3327.
8. Sarginson J, Webb RT, Stocks SJ et al. Temporal trends in antidepressant prescribing to children in UK primary care, 2000–2015. *J Affect Disord*. 2017;210:312–318.

9. Lagerberg T, Molero Y, D'Onofrio BM et al. Antidepressant prescription patterns and CNS polypharmacy with antidepressants among children, adolescents, and young adults: a population-based study in Sweden. *Eur Child Adolesc Psychiatry*. 2019;28(8):1137–1145.
10. Jack RH, Hollis C, Coupland C et al. Incidence and prevalence of primary care antidepressant prescribing in children and young people in England, 1998–2017: A population-based cohort study. *PLoS Med*. 2020;17(7):e1003215. DOI: 10.1371/journal.pmed.1003215.
11. Haapasalo-Pesu KM, Erkolahti R, Saarijärvi S et al. Prescription of psychotropic drugs in adolescent psychiatry wards in Finland. *Nord J Psychiatry*. 2004;58(3):213-218.
12. Cipriani A, Zhou X, Del Giovane C et al. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. *Lancet* 2016;388(10047):881-890.
13. Hintikka U, Viinamäki H, Pelkonen M et al. Clinical recovery in cognitive functioning and self-image among adolescents with major depressive disorder and conduct disorder during psychiatric inpatient care. *Am J Orthopsychiatry*. 2003;73(2):212-222.
14. Lecklin A, Snellman V, Torhola E et al. A retrospective study of hospitalized adolescents suffering from depressive conduct disorder. *Psychiatria Fennica* 2022;53:154-167.
15. Beck AT, Ward CH, Mendelson M et al. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561-571.
16. Beck AT, Weissman A, Lester D et al. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol*. 1974;42(6):861-865.
17. Schorre BEH, Vandvik IH. Global assessment of psychosocial functioning in child and adolescent psychiatry. A review of three unidimensional scales (CGAS, GAF, GAPD). *Eur Child Adolesc Psychiatry*. 2004;13(5):273-286.
18. Zambrowicz R, Stewart JG, Cosby E et al. Inpatient Psychiatric Care Outcomes for Adolescents: A Test of Clinical and Psychosocial Moderators. *Evid Based Pract Child Ment Health*. 2019;4(4):357–368.
19. Setoya Y, Saito K, Kasahara M et al. Evaluating outcomes of the child and adolescent psychiatric unit: A prospective study. *Int J Ment Health Syst*. 2011;5:7.
20. Demircoren BS, Ozbek A, Gencer O. Factors affecting improvement of children and adolescents who were treated in the child and adolescent psychiatry inpatient unit. *J Int Med Res* 2017;45(4):1318–1323.
21. Hayes C, Simmons M, Simons C et al: Evaluating effectiveness in adolescent mental health inpatient units: A systematic review. *Int J Ment Health Nurs*. 2018;27(2):498-513.
22. Vitiello B, Ordóñez AE. Pharmacological treatment of children and adolescents with depression. *Expert Opin Pharmacother*. 2016;17(17):2273-2279.
23. Hetrick SE, McKenzie JE, Bailey AP et al. New generation antidepressants for depression in children and adolescents: a network meta-analysis. *Cochrane Database Syst Rev*. 2021;5(5):CD013674. DOI: 10.1002/14651858.CD013674.pub2.
24. Jilani TN, Gibbons JR, Faizy RM et al. Mirtazapine. In: StatPearls [Internet]. StatPearls Publishing. 2022 [cited 2022 Dec 13]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK519059>

25. Emslie GJ, Wagner KD, Kutcher S, et al. Paroxetine treatment in children and adolescents with major depressive disorder: a randomized, multicenter, double blind, placebo controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2006;45(6):709-719.
26. Le Noury J, Nardo JM, Healy D et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ*. 2015;351:h4320. DOI: 10.1136/bmj.h4320
27. Berard R, Fong R, Carpenter DJ et al. An international, multicenter, placebo controlled trial of paroxetine in adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol*. 2006;16(1-2):59-75.
28. Emslie GJ, Findling RL, Yeung PP et al. Venlafaxine ER for the treatment of pediatric subjects with depression: results of two placebo-controlled trials. *J Am Acad Child Adolesc Psychiatry*. 2007;46(4):479-488.
29. Maan JS, Ershadi M, Khan I et al. Quetiapine. In: StatPearls [Internet]. StatPearls Publishing. 2022 [cited 2022 Dec 13]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459145>
30. National Institute for Health and Care Excellence (NICE). Psychosis and schizophrenia in children and young people: recognition and management. Clinical guideline 155. 2013 [cited 2022 Dec 20]. Available from: <https://www.nice.org.uk/guidance/cg155>
31. Rice F, Riglin L, Lomax T et al. Adolescent and adult differences in major depression symptom profiles. *J Affect Disord*. 2019;243:175-181.
32. Insomnia. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Sleep Research Society. Helsinki: The Finnish Medical Society Duodecim. 2023 [cited 2023 March 31]. Available from: www.kaypahoito.fi



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PSYCHIATRIC INPATIENT TREATMENT OF FOSTERED ADOLESCENTS WITH A DEPRESSIVE DISORDER IS NOT VERY EFFECTIVE

ABSTRACT

This study examined the efficacy of psychiatric inpatient treatment and the use of psychotropic medication in fostered young patients with a depressive disorder. The study sample consisted of 13–17 years old adolescents (n=287) treated due to a depressive disorder in the two adolescent psychiatric units of Kuopio University Hospital, Finland, during the 10-year period 2002–2011. During the study period, there were 299 treatment periods of adolescents living at home and 93 of those placed in foster care. The data concerning demographic and clinical characteristics, treatment outcomes and medication were collected from the patients' medical records. The clinical data revealed that fostered adolescents had more previous psychiatric hospitalizations than their living at home counterparts and their treatment periods were shorter than their non-fostered peers. The decreases of BDI and HS scores from admission to discharge were significantly slighter in fostered adolescents than in their peers. Furthermore, the outcomes of inpatient treatment of severe depression were estimated by the staff teams less often as being satisfactory in fostered adolescents than in those living at home.

KEYWORDS: FOSTERED ADOLESCENTS, DEPRESSIVE DISORDER, PSYCHIATRIC INPATIENT TREATMENT, TREATMENT OUTCOME, PSYCHOPHARMACOLOGICAL MEDICATION

INTRODUCTION

Depression is a common and serious psychiatric disorder in adolescence; the 12-month prevalence has been estimated to be 10.5% among European and 7.5% among US adolescents [1,2]. The disorder is more common among girls, and the prevalence increases as adolescence proceeds [1]. In Finland during 2021, a total of 11210 children were taken into foster care, which corresponded to 1.0% of the nation's children under 18 years of age [3]. In the age group of children over 16 years of age, the share of those in foster care was 2.2% and it was clearly higher than in younger age groups.

The foster care system aims to provide a safe and nurturing environment that meets the needs of children so that they can thrive. However, both during foster care and afterwards, these children seem to fare worse than others [4,5]. Most children in foster care have traumatic family histories and life experiences that result in an increased risk for mental health disorders [6-10] with the most common problems being mood disorders, conduct disorder/oppositional defiant disorder, substance abuse disorder, attention-deficit hyperactivity disorder and anxiety disorder [7,11]. It seems that two-thirds of the hospitalizations of adolescents with a diagnosis of depression end with satisfactory clinical results as estimated by the professional staff (Snellman et al., this journal). However, it is remarkable that only every fourth hospital treatment of adolescents with a depressive conduct disorder ends with satisfactory results [12], and the vast majority (>80%) of these adolescents are living in an institution or in foster care.

When an adolescent ends up in foster care, all of his/her therapeutic needs are not always considered [13]. When the situation in the adolescent's residence suddenly escalates, prompt but sometimes inappropriate solutions are adopted. This study examines psychiatric inpatient treatment, especially psychotropic medication, of the adolescents who had a depressive disorder as a primary psychiatric diagnosis and the outcomes of the hospitalization. Those who arrived from foster care were compared to adolescents coming from elsewhere.

MATERIALS AND METHODS

SAMPLE

The study sample consisted of 13–17 years old adolescents (n=287; 242 females, 45 males) and their 392 inpatient treatment periods due to a depressive disorder in the two

adolescent psychiatric units of Kuopio University Hospital, Finland, during the years 2002–2011. These units serve as a tertiary care centre for the catchment area of North Savo District, which has around one million inhabitants. Both voluntary and involuntary forms of treatment were provided. The treatment was individualized and consisted of therapeutic sessions with a case manager nurse at least once a week, different activities, family sessions, and somatic consultation and psychotropic medication when appropriate [14].

The criteria for inclusion in the study were a duration of hospitalization of at least five days and that data collected via the Beck Depression Inventory questionnaire (BDI) was available at both admission and discharge. The same patient was included several times if he/she had been treated more than once in the adolescent psychiatric units during the years 2002–2011. Some patients had previous psychiatric hospitalization before the year 2002 and therefore none of their treatment periods between 2002–2011 were considered as first ones. Some patients (n=11 with 39 treatment periods) were included in both the fostered and non-fostered groups, since they lived at home during their first inpatient treatment but were fostered later. Similarly, some adolescents (n=19 with 57 treatment periods) were included in several diagnostic groups because they had received different diagnoses from their several hospitalizations.

Data collection and assessment methods

The diagnosis of depression was made in an interview according to ICD-10 (International Classification of Diseases, version 10) criteria as part of the clinical examination performed by a psychiatrist specializing in adolescent care. The patients' diagnoses were categorized into four groups according to the severity of depression diagnosis as follows: 1) mild/moderate depression or cyclothymia (F32.0, F32.1, F33.1, F34.0), 2) severe depression without psychotic symptoms (F32.2, F33.2), 3) severe depression with psychotic symptoms (F32.3, F33.3), and 4) depressive conduct disorder (F92.0).

The demographic and clinical data, including estimations of depressive symptoms (Beck Depression Inventory, BDI), hopelessness (Beck's Hopelessness Scale, HS) and psychosocial functioning (Global Assessment Scale, GAS), were collected from the patients' medical records. These data were collated for the structured forms which were created for the study. Later data was transferred from the forms to Microsoft Excel. This work was done by three Master of Science (Pharmacy) students with their supervisor (AL).

BDI is a numeric self-rated scale used to measure the

severity of depression in a subjective manner [15]. The scores range from zero to sixty-three; higher scores represent more severe depressive symptoms. Scores less than 13 indicate minimal depression, scores from 13 to 18 point to mild depression, scores from 19 to 29 refer to moderate depression and scores from 30 to 63 suggest severe depression. The revised version of BDI from the year of 1996 was used.

HS is a numeric self-rated scale used to measure feelings of pessimism and hopelessness in a subjective manner [16]; its scores range between 0–20. The values under nine refer to mild or insignificant hopelessness whereas a score of fifteen or more represent critical hopelessness.

GAS is a numeric scale used to assess an individual's psychosocial functioning [17]. GAS scores were evaluated by the staff team in the hospital. The scores range from one to a hundred with the scale being divided into ten equal intervals. Low scores indicate poor psychosocial functioning with the upper value of a hundred representing superior functioning. Constant monitoring is needed when an individual's scores are less than 10. Scores less than 41 refer to severe psychosocial functional impairment in several areas whereas scores of 70 or more are regarded as a good functional capacity.

Global Assessment Scale (GAS) and Beck's Hopelessness Scale (HS) were missing from some treatment periods (n=137 and n=125, respectively). In 48% of the inpatient treatments, all three psychiatric assessments (BDI, GAS and HS) at entry and at discharge were obtained from the medical files. Two assessments (BDI and GAS or HS) were found in 37% and one assessment (BDI) in 15% of the inpatient treatments.

Data concerning the efficacy of psychiatric hospitalization, BDI, HS and GAS scores, as well as psychotropic drug therapy, were collected from the medical case summaries. The outcome of treatment was assessed as a dichotomous variable ("satisfactory"/"not satisfactory") and it was based on the estimation of the staff team. The assessment of the treatment outcome, and thus the efficacy of inpatient treatment, was based on BDI, HS and GAS scores as well as on clinical follow-up and the individual goals set in the treatment plan. In addition, the data relating to adverse childhood experiences and comorbid psychiatric disorders were collected from the medical case summaries. The experiences, for example, parental divorce, were "yes" in patients whose medical case summaries stated that the adolescent had experienced it.

STATISTICAL ANALYSES

The data were analysed using the GraphPad Prism program. Continuous variables were categorized as means or medians

and categorical variables as percentages. The statistical significance for categorical variables was analysed using Chi-squared test or Fisher's exact test when the groups were small. The non-parametric Mann-Whitney U test was used for comparisons of continuous variables of independent samples. When comparing more than two groups, Kruskal-Wallis test with the post hoc comparisons with the test of Dunn's Multiple Comparison Test were used. In all analyses, a significance level of $p < 0.05$ was applied.

ETHICAL CONSIDERATIONS

The permission for this study was provided by the ethical committee of Kuopio University Hospital and University of Eastern Finland and by the Medical Director of the University Hospital of Kuopio. Notification of the research was also sent in advance of data collection to the Data Protection Ombudsman.

RESULTS

PATIENT CHARACTERISTICS AND BACKGROUND INFORMATION

There were 299 treatment periods of adolescents living at home that were compared to the 93 hospitalizations of adolescents living in foster care (*Table 1*). Each patient had on average 1.4 (range of 1–9) hospitalizations during the study period. Most patients (79%) were hospitalized only once during the study period. The majority of the adolescents (84%) were female. The adolescents living in foster care had more often adverse childhood experiences compared to their non-fostered counterparts: parents' alcohol or drug abuse (65% vs. 39%, $p < 0.001$); parents' psychiatric disorder (65% vs. 36%, $p < 0.001$); parental divorce (63% vs. 48%, $p < 0.05$); physical abuse (48% vs. 21%, $p < 0.001$); sexual abuse (18% vs. 6%, $p < 0.001$), respectively.

The treatment periods of the adolescents living at home represented their first psychiatric hospitalization significantly more often compared to the fostered adolescents (62% vs. 31%, $p < 0.001$) (*Table 1*). However, 67% of the treatment periods of the adolescents suffering from a severe psychotic depression represented their later hospitalization, regardless of their domestic status (fostered or not).

Comorbid psychiatric disorders were common, particularly in adolescents with mild/moderate depression or cyclothymia (*Table 1*). Neurotic, stress-related and somatoform disorders, as well as mental and behavioural

disorders due to psychoactive substance misuse, were the most common comorbid psychiatric diagnoses in this study.

PSYCHIATRIC INPATIENT TREATMENT

The median length of hospital treatment was 20 days (range 5-369 days). As a whole group, fostered adolescents had shorter treatment periods compared to non-fostered adolescents (median 13 days vs. 21 days, $p<0.001$). Fostered adolescents also had more previous hospitalizations compared to their living at home counterparts. *Table 1* shows results for different diagnostic groups separately.

Positive changes were observed in all psychiatric assessments (BDI, HS, GAS) (*Table 2*). At admission, the majority of the adolescents (61%) had GAS values <40 indicating severe psychosocial functional impairment. At discharge, the psychosocial functioning was still severely impaired more often in fostered adolescents compared to non-fostered counterparts (44% vs. 14%, $p<0.001$). In addition, in the diagnostic group of severe depression without psychotic symptoms, the fostered adolescents had significantly more depressive symptoms at discharge. In line with this, the decreases of BDI and HS scores from admission to discharge were significantly slighter in fostered adolescents than in their peers (*Figure 1*).

At the end of inpatient treatment, the treatment outcome was estimated by the staff team. In most cases, treatment ended with satisfactory clinical results in adolescents suffering from mild/moderate depression or cyclothymia. There were no statistically significant differences in the treatment outcome between fostered and non-fostered adolescents with mild/moderate depression, cyclothymia or depressive conduct disorder. However, in adolescents suffering from severe depression without psychotic symptoms, a clinically satisfactory result was obtained more often in those living at home than in fostered adolescents (72% vs. 41%, $p<0.001$). Similarly, in adolescents suffering from severe depression with psychotic symptoms, the treatment outcome was satisfactory more often in those adolescents living at home in comparison to fostered adolescents (64% vs. 35%, $p<0.05$).

Figure 2 shows the average changes in BDI, HS and GAS assessments between admission and discharge, both in adolescents whose treatment outcome was “satisfactory” and in those whose treatment outcome was “not satisfactory”, estimated by the staff team. There were statistically significant differences in the attenuation of depression symptoms (mainly in BDI) between these patient groups.

Most of the adolescents were receiving psychotropic medication during their hospital stay (*Table 3*) with antidepressants being the drugs most often prescribed. Antipsychotic medications were more often prescribed to fostered adolescents than to their living at home counterparts (73% vs. 52% of treatment periods, $p<0.001$). Quetiapine was the most used psychotropic medicine. It was prescribed mostly due its antipsychotic, antidepressant and mood stabilizing properties. However, in 26% of the prescriptions, it was used in order to help control of anxiety and sleep disorders. In addition, antidepressants were prescribed together with an antipsychotic medication to 37% of the patients. These combinations were administered more commonly to fostered than non-fostered adolescents (47% vs. 34%, $p<0.05$).

Table 1. The characteristics of the study sample

Diagnosis	Mild/moderate depression or cyclothymia		Severe depression without psychotic symptoms		Severe depression with psychotic symptoms		Depressive conduct disorder	
	Fostered adolescents (n=16)	Adolescents living at home (n=69)	Fostered adolescents (n=32)	Adolescents living at home (n=151)	Fostered adolescents (n=17)	Adolescents living at home (n=64)	Fostered adolescents (n=28)	Adolescents living at home (=15)
Gender, female n (%) ^a	14 (88%)	62 (90%)	25 (78%)	134 (89%)	16 (94%)	59 (92%)	21 (75%) *	6 (40%)
First inpatient treatment n (%) ^a	5 (31 %) **	49 (71 %)	10 (31%) ***	103 (68%)	4 (24%)	23 (36%)	10 (36%) *	10 (67%)
Four or more inpatient treatments n (%) ^a	4 (25%) **	3 (4%)	11 (34%) ***	1 (1%)	7 (41%)	14 (22%)	9 (32%) *	0 (0%)
Voluntary treatment n (%) ^a	13 (81%)	61 (84%)	25 (78%)	129 (85%)	8 (47%)	44 (69%)	21 (75%)	7 (47%)
Antidepressant medication at admission n (%) ^a	7 (44%)	23 (33%)	14 (44%)	61 (40%)	10 (59%) *	19 (30%)	12 (43%)	3 (20%)
Antipsychotic medication at admission n (%) ^a	7 (44%)**	9 (13%)	16 (50%) ***	25 (17%)	13 (77%)	38 (59%)	12 (43%) *	1 (7%)
Psychiatric comorbidity n (%) ^a	6 (37%)	26 (38%)	3 (9%)	33 (22%)	4 (24%)	8 (12%)	3 (11%)	3 (20%)
The length of hospitalization, median (range) ^b	15 (6-45)	13 (5-86)	15 (5-67) *	24 (5-96)	19 (5-101)	29 (11-369)	8 (5-60)	16 (5-59)

Statistical significance (fostered adolescents vs. adolescents living at home): *** p<0.001; ** p<0.01; * p<0.05

^a Analysed using Chi-squared test/Fisher's exact test

^b Analysed using Mann-Whitney U test

Table 2. Scores of BDI, GAS and HS of fostered adolescents and adolescents living at home suffering from depressive disorders

Diagnosis	Mild/moderate depression or cyclothymia		Severe depression without psychotic symptoms		Severe depression with psychotic symptoms		Depressive conduct disorder	
	Fostered adolescents (n=16)	Adolescents living at home (n=69)	Fostered adolescents (n=32)	Adolescents living at home (n=151)	Fostered adolescents (n=17)	Adolescents living at home (n=64)	Fostered adolescents (n=28)	Adolescents living at home (n=15)
Severe depression								
BDI ≥ 30 at entry, n (%)	6 (38%)	20 (29%)	22 (69%)	84 (56%)	6 (35%)*	42 (66%)	7 (25%)	3 (20%)
BDI ≥ 30 at discharge, n (%)	1 (6%)	5 (7%)	11 (34%)	39 (26%)	1 (7%)	(25%)	3 (11%)	1 (7%)
Moderate depression								
BDI = 19 – 29 at entry, n (%)	6 (38%)	33 (47%)	7 (22%)	42 (28%)	6 (35%)	15 (23%)	9 (32%)	2 (13%)
BDI = 19 – 29 at discharge, n (%)	3 (19%)	10 (14%)	12 (38%)**	24 (16%)	9 (53%)*	(28%)	5 (18%)	1 (7%)
Mild depression								
BDI = 13 – 18 at entry, n (%)	1 (6%)	11 (16%)	3 (9%)	10 (7%)	2 (12%)	3 (5%)	0 (0%)	3 (20%)
BDI = 13 – 18 at discharge, n (%)	4 (25%)	15 (21%)	2 (6%)	24 (16%)	1 (6%)	12 (19%)	3 (11%)	3 (20%)
Minimal depression								
BDI < 13 at entry, n (%)	3 (19%)	5 (7%)	0 (0%)	15 (10%)	3 (18%)	4 (6%)	12 (43%)	7 (47%)
BDI < 13 at discharge, n (%)	8 (50%)	39 (56%)	7 (22%)*	64 (42%)	6 (28%)	18 (28%)	17 (61%)	10 (67%)
Critical hopelessness								
HS ≥ 15 at entry, n (%)	1 (7%)	13 (19%)	13 (41%)	47 (31%)	7 (41%)	20 (31%)	3 (11%)	1 (7%)
HS ≥ 15 at discharge, n (%)	2 (13%)	4 (6%)	6 (19%)	21 (14%)	4 (24%)	(20%)	3 (11%)	0 (0%)
Severe psychosocial functional impairment								
GAS < 40 at entry, n (%)	12 (75%)	47 (68%)	26 (81%)**	75 (50%)	14 (82%)	45 (70%)	16 (57%)	6 (40%)
GAS < 40 at discharge, n (%)	7 (44%)**	5 (7%)	11 (34%)**	13 (9%)	11 (65%)**	20 (31%)	12 (43%)	4 (27%)

BDI = Beck Depression Inventory, GAS = Global Assessment Scale (missing data n=137, 34.9%), HS = Beck's Hopelessness Scale (missing data n=125, 31.9%); statistical significance (fostered adolescents vs. adolescents living at home): ** p<0.01; * p<0.05; analysed using Chi-squared test/Fisher's exact test

Table 3. Psychotropic medication used in the inpatient care of fostered adolescents and adolescents living at home suffering from depressive disorders

Diagnosis	Mild/moderate depression or cyclothymia		Severe depression without psychotic symptoms		Severe depression with psychotic symptoms		Depressive conduct disorder	
	Fostered adolescents (n=16) n (%)	Adolescents living at home (n=69) n (%)	Fostered adolescents (n=32) n (%)	Adolescents living at home (n=151) n (%)	Fostered adolescents (n=17) n (%)	Adolescents living at home (n=64) n (%)	Fostered adolescents (n=28) n (%)	Adolescents living at home (n=15) n (%)
Psychotropic medication	16 (100 %)	57 (83%)	31 (97%)	146 (97 %)	17 (100%)	63 (98%)	24 (86 %)	10 (67%)
Antidepressant	11 (69%)	42 (61%)	25 (78%)	130 (86%)	10 (59%)	36 (56%)	17 (61%)	7 (47%)
Antipsychotic	13 (81%) ***	23 (33%)	22 (69%) *	69 (46%)	16 (94%)	61 (95%)	17 (61%) *	3 (20%)
Antidepressant + antipsychotic	8 (50%) **	12 (17%)	16 (50%)	55 (36%)	9 (53%)	33 (52%)	11 (39%)	2 (13%)
Anxiolytic	8 (50%) *	14 (20%)	16 (50%)	48 (32%)	9 (53%)	41 (64%)	5 (18%)	3 (20%)
Sedative	9 (56%)	28 (40%)	12 (37%)	58 (38%)	5 (29%)	31 (48%)	7 (25%)	5 (33%)
Other ^a	0 (0%)	1 (1%)	2 (6%)	3 (2%)	1 (6%)	5 (8%)	1 (4%)	0 (0%)

^a includes lamotrigine (n=7), valproic acid (n=3), methylphenidate (n=1), naltrexone (n=1) and topiramate (n=1); statistical significance (fostered adolescents vs. adolescents living at home): *** p<0.001; ** p<0.01; * p<0.05; analysed using Chi-squared test/Fisher's exact test

Figure 1. The average changes of BDI, HS and GAS scores of fostered adolescents and adolescents living at home. The changes of BDI and HS scores represent the decrease of those scores between the admission and the discharge. Conversely, the changes of GAS scores represent the increase of those scores

BDI = Beck Depression Inventory, HS = Beck's Hopelessness Scale, GAS = Global Assessment Scale
Statistical significance (fostered adolescents vs. adolescents living at home): *** $p < 0.001$; * $p < 0.05$
Analysed using Mann-Whitney U test

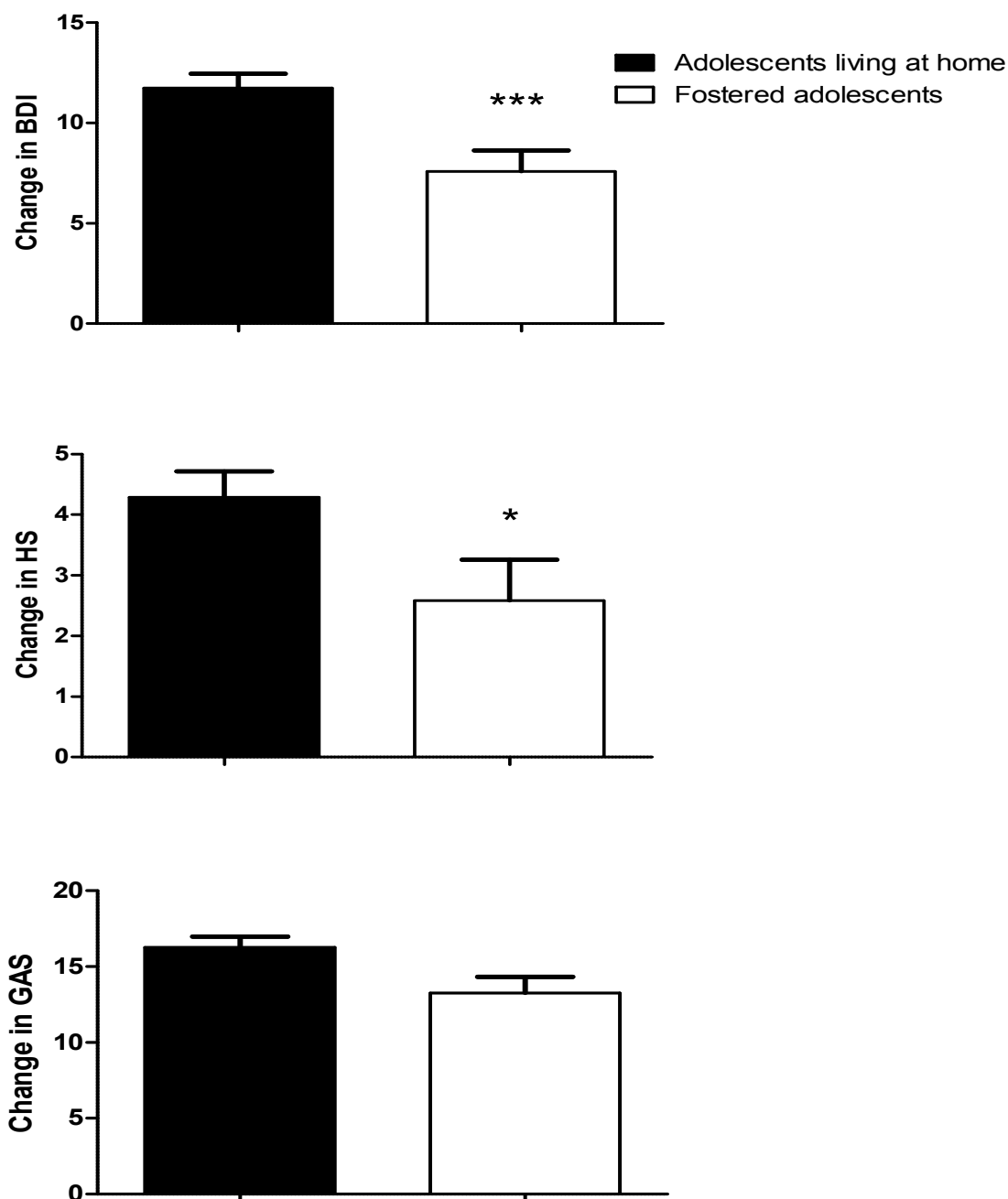
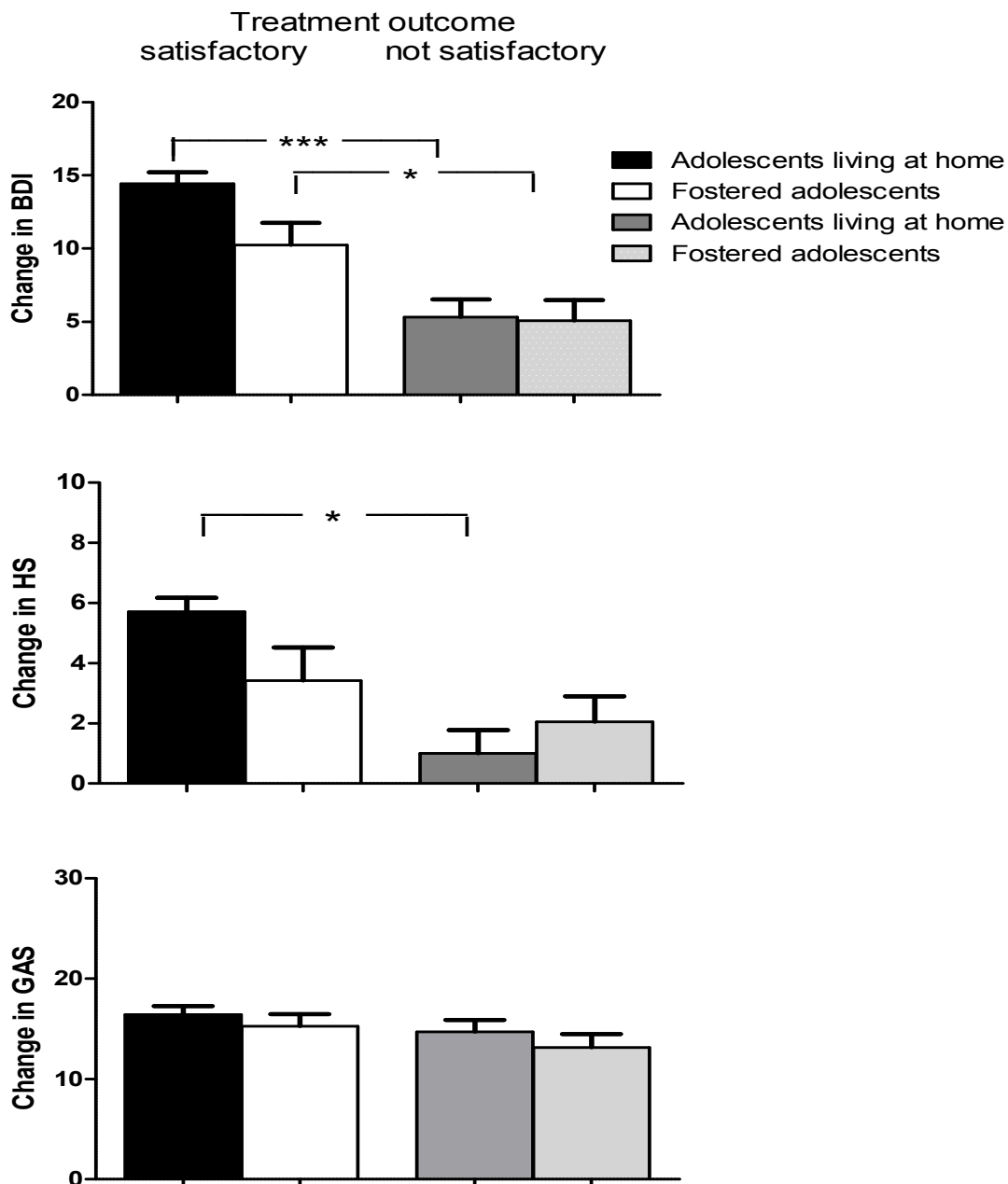


Figure 2. The average changes of BDI, HS and GAS scores of fostered adolescents and adolescents living at home in cases of satisfactory and not satisfactory treatment outcome. The changes of BDI and HS scores represent the decrease between the admission and the discharge. Conversely, the changes of GAS scores represent the increase of those scores.

BDI = Beck Depression Inventory, HS = Beck's Hopelessness Scale, GAS = Global Assessment Scale
Statistical significance (satisfactory vs. not satisfactory): *** $p < 0.001$; * $p < 0.05$
Analysed using Kruskal-Wallis test



DISCUSSION

This clinical data shows that adolescents placed in foster care and suffering from depressive disorders had more previous hospitalizations than their counterparts. They also had often an antipsychotic medication both at admission and during their hospital stay. According to the assessments of the staff teams, a clinically satisfactory result was achieved less often in fostered adolescents suffering from severe depression (either psychotic or non-psychotic) when compared to treatment outcomes of the adolescents living at home. Furthermore, the length of the inpatient treatments were shorter in fostered adolescents. The subjective feelings of hopelessness and depression relieved less in fostered adolescents compared to those living at home. This, and the fact that almost half of the fostered adolescents were still experiencing severely impaired psychosocial functioning at discharge, indicates that these adolescents remained particularly vulnerable to the manifestations of mental health problems and the need for subsequent rehospitalizations [18,19].

Fostered children and adolescents have often experienced different types of maltreatment and a lack of stability in their childhood [20]. According to our study, the adolescents living in foster care had also experienced more often adverse childhood experiences such as a parent's alcohol or drug abuse and/or parents' psychiatric problems and physical/sexual abuse compared to their living at home counterparts. It is known that traumatic life experiences in childhood may increase the risk of mental health disorders and the need for mental health services and psychotropic medication [21,22]. It has also been reported that adolescents in foster care exhibit more psychiatric symptoms than their non-fostered peers [23]. Overall, comorbid psychiatric disorders were particularly common in adolescents (fostered or not) with mild/moderate depression or cyclothymia. These patients can usually be treated in outpatient care, but hospitalization may have been needed, e.g., due to psychiatric comorbidities, suicidality, severe impairment in psychosocial functioning or inadequate outpatient care.

Here, depressed adolescents placed in foster care had more previous psychiatric inpatient treatments compared to adolescents living at home. Fostered adolescents also had shorter psychiatric inpatient treatment and many of them were discharged with severely impaired psychosocial functioning, according to their GAS scores. Furthermore, the treatment outcomes of fostered adolescents with severe depression were more often estimated being “not

satisfactory” when compared to the treatment outcomes of their counterparts. It should be noted that some of the fostered adolescents had lived at home during their first inpatient treatment(s) and were fostered later, implying possibly an already complicated situation. The management of acute crises may have been the aim of the inpatient care in some challenging cases. In addition, inadequate outpatient psychiatric treatment or unstable foster care placement may also have been reasons for several hospitalizations. It's noteworthy that the comprehensive care of the adolescents with severe psychiatric symptoms consists of the different kinds of intervention of adolescent psychiatry, school and child welfare.

It is also important to invest in stable foster care combined with adequate psychiatric outpatient care, modified to the needs of each adolescent. Untreated mental health disorders may have long-term consequences for an individual. Adolescents who have experienced trauma are more likely to demonstrate externalizing behaviours, including disruptive or impulsive behaviour or conduct disorders, and fostered adolescents more likely demonstrate these kinds of behaviours upon placement [24]. Externalizing behaviours are a risk factor for the adolescent to have an increased number of changes in his/her foster care placements. Furthermore, placement instability increases the risk for continued mental health problems into adulthood [20].

Most of the young patients received psychotropic medication, particularly antidepressants, during their hospital stay. Overall, antipsychotic medications were more often prescribed to fostered adolescents than to their counterparts. Antipsychotics are administered to adolescents, e.g., in the treatment of severe depression, bipolar disorder and disruptive and aggressive behaviours such as conduct disorder [25-27]. They can also be combined with antidepressants in the treatment of psychotic depression [25]. These combinations were prescribed more often to fostered than non-fostered adolescents in our study. Quetiapine was the most often administered medication; this drug was also used in order to help control behavioural problems, anxiety and sleep disorders. Higher usage rates of psychotropic medications of fostered adolescents have also been reported previously [28,29]. According to the reports of dosReis et al. [29], Raghavan et al. [30] and Zito et al. [31], adolescents placed in foster care often were being treated with multiple concurrent psychotropic medications. Regardless of the indication, possible adverse events of psychotropic medications, such as psychiatric and metabolic effects, must be considered and monitored carefully [25,32].

Fostered adolescents have often suffered adverse childhood experiences which will significantly impact on their entire lives. Several hospitalizations and inadequate treatment outcomes may also have many negative long-term effects on the course of an individual's life. Adults with a history of foster care do seem to struggle in multiple areas in comparison to their peers [5,20].

LIMITATIONS

The present study has some limitations. It was a retrospective study investigating the efficacy of inpatient treatment in fostered adolescents suffering from a depressive disorder, and the use of psychotropic medication during their hospitalization. The data were collected from patients' medical records which had not been written for scientific purposes. Some patients (n=11 with 39 treatment periods) were included in both the fostered and non-fostered groups since they lived at home during their first inpatient treatments but were fostered later. Similarly, some adolescents (n=19 with 57 treatment periods) were included in several diagnostic groups because they had received different diagnoses in their several hospitalizations. In addition, data of GAS and HS scores were missing from some treatment periods (n=137 and n=125, respectively). However, this method may obtain more authentic results than possibly with other approaches, such as interviews, because our data are based on the medical records written by professional staff.

The psychiatric diagnoses were made by psychiatrists who applied the ICD-10 diagnostic system without any structured interview, which would have been more reliable. Furthermore, we had no access either to the adolescents' outpatient information or to their inpatient data with respect to any treatment periods before the study period (2002–2011). If this missing information had been available, it would have been possible to gain a wider perspective of the treatment of depressed adolescents.

CONCLUSIONS

In conclusion, it is demanding to treat adolescents with a depressive disorder, especially if they are arriving from foster care. Fostered adolescents often are burdened by a traumatic family history and life experiences which significantly affect their entire lives. It seems that inpatient treatment of these adolescents is less beneficial compared to their non-fostered counterparts. The hospitalization of fostered adolescents can be only one part of their

comprehensive care. Therefore, it is important to invest in stable foster care combined with adequate psychiatric outpatient care tailored to the needs of each individual adolescent.

Disclosures

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References

1. Avenevoli S, Swendsen J, He J et al. Major depression in the national comorbidity survey-adolescent supplement: prevalence, correlates, and treatment. *J Am Acad Child Adolesc Psychiatry*. 2015;54(1):37–44.
2. Balázs J, Miklósi M, Keresztény A et al. Adolescent subthreshold-depression and anxiety: psychopathology, functional impairment and increased suicide risk. *J Child Psychol Psychiatry*. 2013;54(6):670–677.
3. Forsell M, Kuoppala T. Child welfare 2021. The number of children taken into care continued to decline in 2021. Finnish Institute for Health and Welfare, Statistical report 22/2022.
4. Pecora PJ, Jensen PS, Hunter Romanelli L et al. Mental health services for children placed in foster care: an overview of current challenges. *Child Welfare*. 2009;88(1):5-26.
5. Sariaslan A, Kääriälä A, Pitkänen J et al. Long-term health and social outcomes in children and adolescents placed in out-of-home care. *JAMA Pediatr*. 2022;176(1):e214324. doi:10.1001/jamapediatrics.2021.4324
6. Dubois-Comtois K, Bussièrès EL, Cyr C et al. Are children and adolescents in foster care at greater risk of mental health problems than their counterparts? A meta-analysis. *Child Youth Serv Rev*. 2021;127:1-11.
7. Engler AD, Sarpong KO, Van Horne BS et al. A Systematic Review of Mental Health Disorders of Children in Foster Care. *Trauma Violence Abuse*. 2022;23(1):255-264. doi: 10.1177/1524838020941197
8. Hurlburt MS, Leslie LK, Landsverk J et al. Contextual predictors of mental health service use among children open to child welfare. *J Arch Gen Psychiatry*. 2004;61(12):1217-1224. doi: 10.1001/archpsyc.61.12.1217
9. Minnis H, Everett K, Pelosi AJ et al. Children in foster care: mental health, service and costs. *Eur Child Adolesc Psychiatry*. 2006;15(2):63-70. doi: 10.1007/s00787-006-0452-8
10. McMillen JC, Scott LD, Zima BT et al. Use of mental health services among older youths in foster care. *Psychiatr Serv*. 2004;55(7):811-817. doi: 10.1176/appi.ps.55.7.811
11. Kääriälä A, Gyllenberg, Sund R. The association between treated psychiatric and neurodevelopmental disorders and out-of-home care among Finnish children born in 1997. *Eur Child Adolesc Psychiatry*. 2022;31(11):1789-1798.
12. Lecklin A, Snellman V, Torhola E et al. A retrospective study of hospitalized adolescents suffering from depressive conduct disorder. *Psychiatria Fennica* 2022;53:154-167.
13. Koponen N, Laukkanen E, Tolmunen T et al. Joutuvatko sijaishuoltopaikkojen nuoret liian herkästi nuorisopsykiatriselle osastolle? *SLL* 2010;65(49):4073-4078.
14. Hintikka U. Changes in Adolescents' Cognitive and Psychosocial Functioning and Self-Image During Psychiatric Inpatient Treatment. Dissertation. Kuopio University Publications, Kuopio, Finland, 2007.
15. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clin Psychol Rev*. 1988;8:77-100.
16. Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the Hopelessness Scale. *J Consult Clin Psychol*. 1974;42:861–865.

17. Schorre BEH, Vandvik IH. Global assessment of psychosocial functioning in child and adolescent psychiatry. A review of three unidimensional scales (CGAS, GAF, GAPD). *Eur Child Adolesc Psychiatry*. 2004;13(5):273-286. doi: 10.1007/s00787-004-0390-2
18. Endicott J, Spitzer RL, Fleiss JL et al. The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976;33(6):766-771.
19. Zambrowicz R, Stewart JG, Cosby E et al. Inpatient psychiatric care outcomes for adolescents: A test of clinical and psychosocial moderators. *Evid Based Pract Child Adolesc Ment Health*. 2019;4(4):357-368. doi: 10.1080/23794925.2019.1685419
20. Gypen L, Vanderfaeillie J, De Maeyer S. Outcomes of children who grew up in foster care: systematic-review. *Child Youth Serv Rev*. 2017;76:74-83.
21. Björkenstam E, Hjern A, Mittendorfer-Rutz E et al. Multi-exposure and clustering of adverse childhood experiences, socioeconomic differences and psychotropic medication in young adults. *PLoS One*. 2013;8(1):e53551. doi: 10.1371/journal.pone.0053551
22. Alcalá HE, Balkrishnan R. Mental health services in childhood: the role of family adversity. *Public Health Rep*. 2019;134(2):180-188. doi: 10.1177/0033354919826555
23. Mekonnen R, Noonan K, Rubin D. Achieving Better Health Care Outcomes for Children in Foster Care. *Pediatr Clin North Am*. 2009;56(2):405-415. doi: 10.1016/j.pcl.2009.01.005
24. Lohr WD and Jones VF. Mental Health Issues in Foster Care. *Pediatr Ann*. 2016;45(10):e342-e348. doi: 10.3928/19382359-20160919-01
25. Depression. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Psychiatric Association. Helsinki: The Finnish Medical Society Duodecim, 2023 (referred April 25, 2023). Available online at: www.kaypahoito.fi
26. Conduct Disorders (children and adolescents). Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, the Finnish Society for Child Psychiatry, the Finnish Society for Adolescent Psychiatry and the Finnish Psychiatric Association. Helsinki: The Finnish Medical Society Duodecim, 2018 (referred April 25, 2023). Available online at: www.kaypahoito.fi
27. Bipolar disorder. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, the Finnish Psychiatric Association and the Finnish Society for Adolescent Psychiatry, the Finnish Society for Adolescent Psychiatry. Helsinki: The Finnish Medical Society Duodecim, 2021 (referred August 24, 2023). Available online at: www.kaypahoito.fi
28. Raghavan R, Zima BT, Andersen RM et al. Psychotropic medication use in a national probability sample of children in the child welfare system. *J Child and Adolesc Psychopharmacol*. 2005;15(1):97-106. doi:10.1089/cap.2005.15.97
29. dosReis S, Yoon Y, Rubin DM et al. Antipsychotic treatment among youth in foster care. *Pediatrics*. 2011;128(6):e1459–e1466. doi:10.1542/peds.2010-2970
30. Raghavan R, McMillen JC. Use of multiple psychotropic medications among adolescents aging out of foster care. *Psychiatr Serv*. 2008;59(9):1052-1055. doi:10.1176/ps.2008.59.9.1052.

31. Zito JM, Safer DJ, Sai D et al. Psychotropic medication patterns among youth in foster care. *Pediatrics*. 2008;121(1):e157-163. doi:10.1542/peds.2007-0212
32. Schizophrenia. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Psychiatric Association. Helsinki: The Finnish Medical Society Duodecim, 2022 (referred May 8, 2023). Available online at: www.kaypahoito.fi



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A 10-YEAR TIME TREND ANALYSIS OF ELDERLY PATIENTS IN PSYCHOGERIATRIC WARD IN OULU UNIVERSITY HOSPITAL

ABSTRACT

Psychiatric disorders are relatively common in the elderly, and prevalence of these disorders is parallel to or greater than in younger cohorts. The aim of this study was to examine a 10-year time trend in inpatient episode data of elderly patients, who were treated in the psychogeriatric ward at Oulu University Hospital during 1.1.2012-31.12.2021. Major focuses were on gender differences and inpatient days in main psychiatric diagnoses among patient groups by age: 65-74 years old (young-old), 75-84 years old (middle-old) and >85 years old (oldest-old).

A total of 1034 psychogeriatric inpatient episodes were reported in the study period. 755 (73%) of inpatient episodes were in women and 279 (27%) in men. The proportion of young-old patients significantly decreased (trend test, $p=0.009$), while those of middle-old patients remained rather stable ($p=0.689$). In oldest-old patients, an increasing trend was observed ($p=0.182$), particularly from year 2017 onwards ($p=0.074$). Among the main three diagnostic groups, affective disorders were the most common, forming 50.8% of diagnoses, followed by psychotic disorders (28.7%) and anxiety disorders (10.5%). The distribution of psychiatric main diagnostic categories was the same in all age groups, except among oldest-old men, in which psychotic disorders were more common than in other age groups. Among age groups, middle-old men with affective disorder diagnosis had longer inpatient episodes than same age women (36.4 days vs. 28.3 days, $p=0.013$).

Our study also illustrates the need for better means to identify age-related and varied causes of elderly patients being admitted to psychogeriatric wards. These elderly patient groups may need different mental health services in young-old age than in oldest-old age. Elderly persons are known to benefit from timely treatment. Longer delay in appropriate care can lead to greater loss of level of daily functioning in the elderly.

KEYWORDS: GERIATRIC PSYCHIATRY, GENDER DIFFERENCES, DEPRESSION, ANXIETY, PSYCHOSIS, INPATIENT EPISODE, ELDERLY

INTRODUCTION

Psychiatric disorders are relatively common in the elderly, and they associate with several social and demographic variables, e.g., age, gender, marital status, education and social support [1] as well as somatic conditions [2,3]. Furthermore, psychiatric disorders may decrease quality of life and even increase mortality [4].

The prevalence of psychiatric disorders among the elderly is equal to or greater than in younger subjects [5,6]. Some estimates suggest that the overall prevalence of psychiatric disorders in the elderly without dementia may be as high as 20-30% [7,8]. Psychiatric comorbidity is also very common. For example, a comorbidity of 50-90% has been reported between depression and anxiety disorders [8].

Depression is a prevalent psychiatric disorder and a common cause of disability among the elderly [9]. The prevalence of depression has varied largely in different studies due to methodological differences. Sjöberg et al. [9] established a 4.2% prevalence of any depression for ICD-10. In addition, 10 to 15% of the elderly are found to exhibit less severe depressive symptoms, not diagnosed as depressive disorders [10]. A review article by Djernes [3] established that female gender, somatic illness, widowhood and a history of depression may be risk factors for depression in the elderly. According to their findings, depression in old patients is often poorly recognized and treated [3].

Anxiety disorders typically develop between childhood and young adulthood. Compared to younger cohorts, lifetime prevalence of anxiety disorders is lower in the elderly [11]. Wolitzky-Taylor et al. [11] have reported that prevalence of anxiety disorders varies by age-specific subgroups within the elderly population from 3.2 to 14.2%, with lowest prevalence reported in the subgroups aged <65 and >85 and highest in the subgroup aged 65-85. Furthermore, anxiety is found to be common among geriatric psychiatric patients and associated with, for example, severity of depression and female gender [12].

Like depression and anxiety, psychotic symptoms and psychotic disorders are relatively common in the elderly population [13,14]. Prevalence is dependent on age, for example, Skoog [8] reports that psychotic disorders are considerably more common among people aged between 85 and 95 than in younger cohorts. Skoog [8] suggests that those aged 70 have a prevalence of 1% for psychotic symptoms whereas the prevalence in older age groups is much higher, 10% and 8% in patients aged 85 and 95, respectively. Psychotic symptoms, e.g., schizophrenia, delusional disorders and

schizoaffective disorders, may arise from a primary psychotic disorder or be of secondary origin.

Geriatric psychiatry is a subspecialty of psychiatry, which concentrates on the assessment and treatment of elderly patients [14]. Further, geriatric psychiatric wards are a limited resource in psychiatric hospitals [15]. Previous studies have established that several factors affect the length of stay in hospital among elderly patients, like age, gender and living alone. Furthermore, number of recent psychiatric admissions, involuntary admission and close or constant observation level predict longer hospital length of stay in geriatric patients [1,16]. Previous studies have dealt with factors predicting hospitalization among the elderly population, but there is a lack of studies concerning inpatient episodes among elderly psychiatric inpatients.

The proportion of the elderly, more precisely those of over 65 years of age, has increased in the total population of the world. This trend has some important implications over many fields of society, including healthcare [17]. The elderly population's need for primary and specialized mental health services, as well as welfare and social services, has been recognized in the wellbeing services counties [18]. Further research in psychiatric hospitalization is necessary for study among elderly subjects, planning new psychiatric and health services for the growth of the elderly population [19].

The aim of this study was to examine the 10-year time trend of elderly patients needing inpatient hospitalization in the psychogeriatric ward at Oulu University Hospital during years 2011–2021. Major focuses were on gender differences and inpatient days in main psychiatric diagnoses among patients in three age groups. Patients were divided by Erber's classification [20] in groups by age: 65-74 years old (young-old), 75-84 years old (middle-old) and >85 years old (oldest-old).

DATA SOURCES

STUDY SAMPLE

This register-based study analysed 10-year inpatient episode data of elderly patients, who were treated in the psychogeriatric ward at Oulu University Hospital during 1.1.2012-31.12.2021. The psychogeriatric ward is the only psychiatric ward specialized in psychiatric disorders for patients over 65 years old in the catchment area of Oulu University Hospital in Northern Finland, covering the Wellbeing Services Counties of North Ostrobothnia (Pohde) and Lapland (Lapha). It has 12 inpatient beds for voluntary

and involuntary admissions, except during a three-month period from January to March 2012 (9 beds). During the years 2012-2018, the length of ward closure varied from eight to 66 days. From year 2019 onwards, the ward has been open 24/7 every day of the year [21].

Specialized level psychiatric inpatient care is supposed to offer treatment to patients with psychiatric illness by a multi-professional team (psychiatrist, nurses, psychologist, social worker, occupational therapist, physiotherapist). Besides treating underlying psychiatric diagnoses, it is also necessary to take care of severe somatic comorbidity of the patients. Psychogeriatric inpatient care is based on individual needs, constituting nurse-patient relationships and on-ward events, like different therapeutic groups, medication and, when necessary, methods of neuromodulation, such as transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS) and electroconvulsive therapy (ECT).

The initial data included 1078 episodes. Those occurring with patients aged under 65 years old ($n=44$, 4.1%) were excluded from further analysis. Thus, the final data of elderly patients comprised 1034 inpatient episodes.

VARIABLES

The sociodemographic characteristics included gender (female, male) and age of patients. Patients were categorized according to Erber [20] into three age groups: 65-74 years old (young-old), 75-84 years old (middle-old) and >85 years old, (oldest-old).

Our study analyses the primary diagnosis of patients recorded in inpatient episodes. These diagnoses were based on the International Classification of Diseases, tenth revision (ICD-10) [22]. The psychiatric diagnoses were categorized into seven major groups: 1) Organic mental disorders (F0-09), 2) Substance use disorders (F10-19), 3) Psychotic disorders (F20-29), 4) Affective disorders (F30-39), 5) Anxiety disorders (F40-49), 6) Behavioural syndromes associated with physiological disturbances and physical factors and 7) Personality disorders (F60-69). Furthermore, the rest of the diagnoses were analysed in the groups for neurological (G20-G39) and other somatic diagnoses.

The approval for the use of the inpatient episode data for research purposes was obtained from the department of psychiatry at Oulu University Hospital (Permission 9/2023, 19.1.2023).

STATISTICAL ANALYSIS

The statistical significance of group differences in the categorical variables were examined with Pearson's Chi-squared or Fisher's Exact test. All statistical tests were two-tailed and the limit for statistical significance was set at $p<0.05$. The statistical software used in analyses was IBM SPSS Statistics, version 26.

RESULTS

A total of 1034 inpatient episodes were reported for elderly patients treated in the ward of geriatric psychiatry at Oulu University Hospital between 2012-2021. As seen in *Table 1*, 755 (73%) of inpatient episodes were in women and 279 (27%) in men. During this 10-year study period, the annual number of inpatient episodes varied between 87-123 days. The median length of stay varied annually between 22-35 days.

Table 1. Ten-year inpatient episode statistics for elderly patients treated in the psychogeriatric ward at Oulu University Hospital

Year	Number of Inpatient episodes			Length of stay (in days) in psychogeriatric unit			
	Total data	Women n (%)	Men n (%)	sum	median	25 percentile	75 percentile
2012	103	74 (71.8)	29 (28.2)	3137	25	8	42
2013	105	70 (66.7)	35 (33.3)	2489	22	12	35
2014	87	63 (72.4)	24 (27.6)	2937	28	16	48
2015	97	76 (78.4)	21 (21.6)	3299	32	13	46
2016	92	72 (78.3)	20 (21.7)	3226	34	12	48
2017	123	90 (73.2)	33 (26.7)	3567	23	7	39
2018	99	73 (73.7)	26 (26.3)	3770	32	21	50
2019	111	79 (71.2)	32 (28.8)	4089	29	15	49
2020	106	73 (68.9)	33 (31.1)	4041	35	17	49
2021	111	85 (76.5)	26 (23.4)	3697	26	17	41
Total 2012-2021	1034	755 (73.0)	279 (27.0)	34252	28	14	45

During 2012-2018 the length of unit closure varied from 8 to 66 days.
During 2019-2021 the ward was open every day of the year

Among all elderly inpatient episodes in the 10-year time period, 409 (39.6%) were young-old, 510 (49.3%) middle-old and 115 (11.1%) oldest-old. As *Figure 1* shows, during the 10-year time period the proportion of young-old patients significantly decreased (trend test, $p=0.009$), while that of middle-old patients remained rather stable ($p=0.689$). In oldest-old patients, an increasing trend was observed ($p=0.182$), particularly from year 2017 onwards ($p=0.074$).

Figure 1. Percentages of all inpatient episodes among elderly patients in years 2012-2021

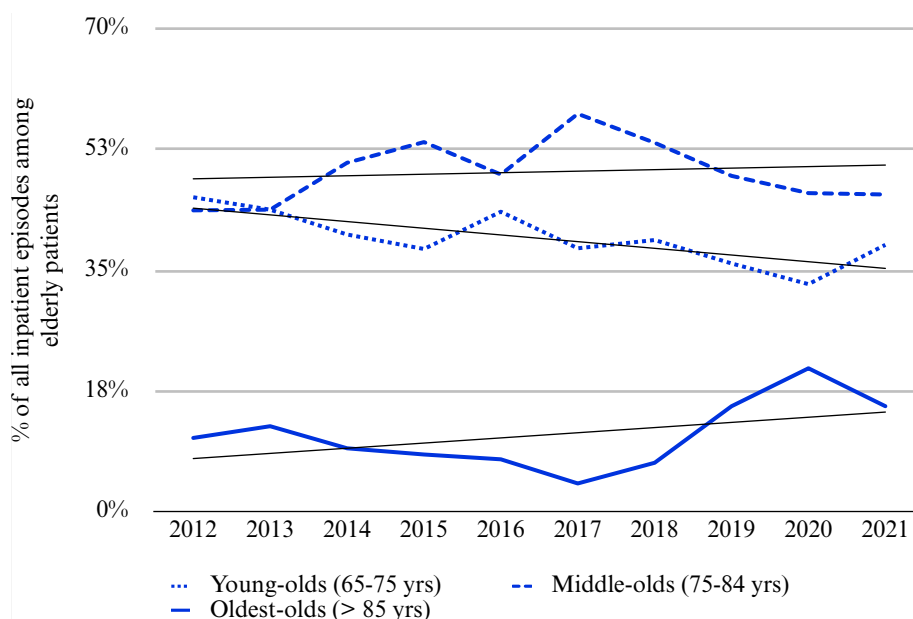


Table 2 presents the most common psychiatric diagnoses in inpatient episodes by main diagnostic groups. Psychiatric diagnoses covered the majority (93.6%) of all diagnoses set in inpatient episodes. In the main three diagnosis groups, affective disorders were the most common, forming 50.8% of diagnoses, followed by psychotic disorders (28.7%) and anxiety disorders (10.5%). The rest of psychiatric diagnoses covered 4.2% of all main diagnoses. Neurological disorders (G20-G39) were recorded in 5.1% and other somatic disorders were 1.3% of all inpatient episodes. The distribution of psychiatric main diagnostic categories was the same in all age groups, except among oldest-old men, in which psychotic disorders were more common than in other age groups.

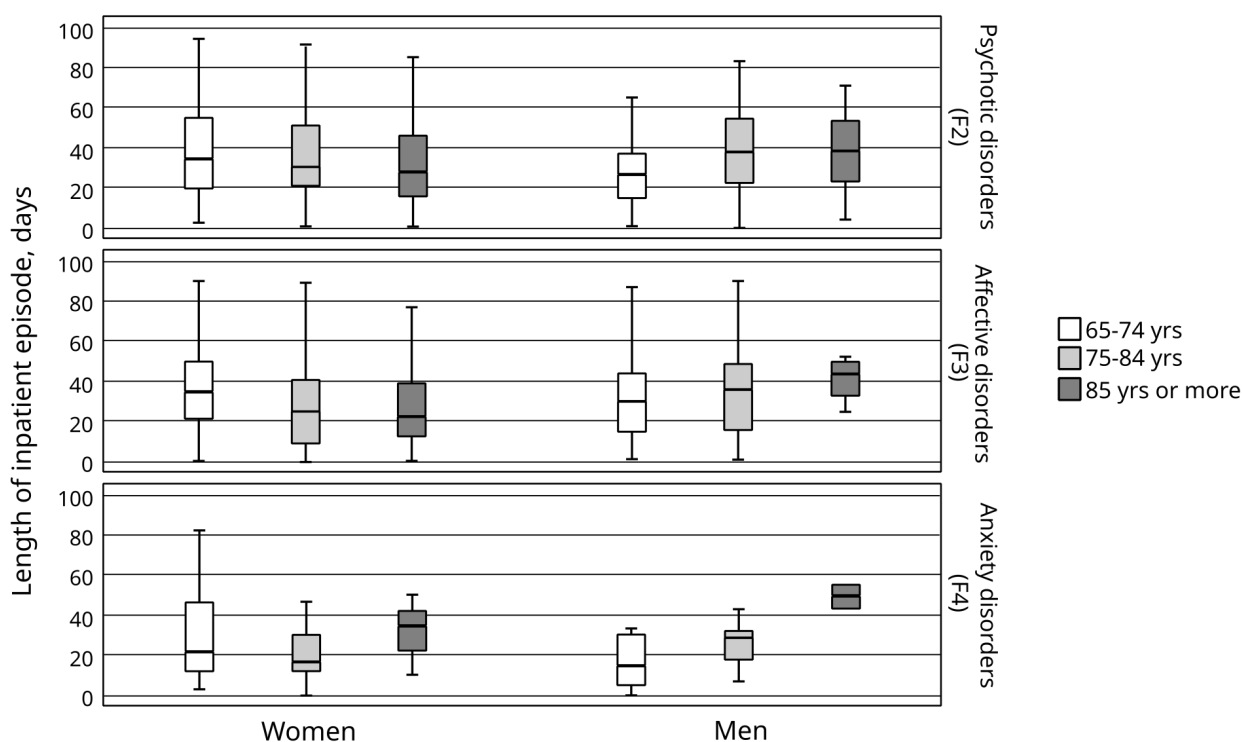
Table 2. The prevalence of main diagnoses (ICD-10) assessed in inpatient episodes by gender and age groups

	Total data n (%)	All age groups(n=1034)		65-74 years (n=409)		75-84 years (n=510)		85 > years (n=115)	
		Women n (%)	Men n (%)	Women n (%)	Men n (%)	Women n (%)	Men n (%)	Women n (%)	Men n (%)
Psychiatric diagnoses									
Organic mental disorders	33 (3.2)	25 (33.1)	8 (2.9)	10 (3.6)	1 (0.7)	10 (2.6)	5 (4.0)	5 (5.3)	2 (9.5)
Substance use disorders	2 (0.2)	1 (0.1)	1 (0.4)	1 (0.4)	1 (0.7)	0	0	0	0
Psychotic disorders	291 (28.7)	208 (27.5)	83 (29.7)	102 (37.1)	38 (28.4)	80 (20.7)	33 (26.6)	26 (27.7)	12 (57.1)
Affective disorders	525 (50.8)	390 (51.7)	135 (48.4)	116 (42.2)	60 (44.8)	225 (58.3)	71 (57.3)	49 (52.1)	4 (19.0)
Anxiety disorders	109 (10.5)	94 (12.5)	15 (5.4)	34 (12.4)	8 (5.9)	56 (14.5)	5 (4.0)	4 (4.0)	2 (9.5)
Behavioural syndromes	2 (0.2)	2 (0.2)	0	0	0	1 (0.3)	0	1 (1.1)	0
Personality disorders	6 (0.6)	2 (0.2)	4 (1.4)	2 (0.8)	2 (1.4)	0	2 (1.6)	0	0
Psychiatric diagnoses Total	970 (93.6)	722 (95.6)	246 (88.2)	265 (96.4)	110 (82.1)	372 (96.4)	116 (93.5)	85 (90.4)	20 (95.3)
Somatic diagnoses									
Neurological disorders	53 (5.1)	24 (3.2)	29 (10.4)	6 (2.2)	23 (17.2)	11 (2.8)	5 (4.0)	7 (7.4)	1(4.7)
Other somatic disorders	13 (1.3)	9 (1.2)	4 (1.4)	4 (1.5)	1 (0.4)	3 (0.8)	3 (2.4)	2 (2.1)	0
Somatic diagnoses Total	66 (6.4)	33 (4.4)	33 (11.8)	10 (3.6)	24 (17.9)	14 (3.6)	8 (6.5)	9 (9.6)	1 (4.7)
Total	1034	755 (100)	279 (100)	275 (100)	134 (100)	386 (100)	124 (100)	94 (100)	21 (100)

Figure 2 visualizes the average length (days) of stay of inpatient episodes in main psychiatric diagnoses by gender and age groups of elderly patients. In psychotic disorders, the average length of stay between age groups varied from 33.0 to 46.7 days in men ($p=0.210$) and from 35.3 to 41.1 days in women ($p=0.644$). In affective disorders, the length of stay between age groups varied from 36.4 to 41.3 days in men ($p=0.941$) and from 27.9 to 39.5 days in women ($p<0.001$). Further, in anxiety disorders, the length of stay between age groups varied from 16.8 to 49.5 days in men ($p=0.026$) and from 23.2 to 33.3 days in women ($p=0.270$).

In additional analysis, a significant difference between genders was found in affective disorders in which men had longer inpatient episodes (36.6 days) compared to women (31.5 days, $p=0.048$). Among the age group middle-old, men with affective disorders had longer inpatient episodes than same age women (36.4 days vs. 28.27 days, $p=0.013$).

Figure 2. Length of inpatient episode (days) in age groups and in main diagnoses



DISCUSSION

The results of our 10-year time trend data of elderly psychiatric inpatients show that the proportion of all hospital episodes that had increased the most was among the oldest-old patients, over 85 years old, in the 10-year study period, particularly from year 2017 onwards. Middle-old and oldest-old patient groups in this study had more inpatient episodes than the proportion of those age groups in the general population [23]. Our finding is in line with a previous Finnish follow-up study, in which depressiveness was found to increase in women from age 80 to 85 years and that men reached the same depressive symptoms at an earlier age than women [24]. A French study by Parent et al. [25] reported that the population of very old patients is increasing and they require appropriate high quality care and prolonged hospitalization. Ageing and a longer life increases risk of experiencing negative consequences, like physical and mental disorders and social isolation [26], which inevitably increases the need for various healthcare services focused on the elderly population.

Affective disorders were the most common diagnoses in our study, accounting for half of the diagnoses in inpatient episodes in all age groups, except oldest-old male patients. Our finding is in line with previous studies, in which depression in old age has been found to be common among the elderly and also to associate with psychiatric inpatient service utilization [10,27]. In our study, female patients represented the majority of patients treated during the whole ten-year study period. This result is in agreement with earlier research, reporting affective disorders more in women than men [3]. Furthermore, the average length of stay in women was longer in the young-old group compared to older women. One possible reason for this finding may be that those young-old patients may have had more often severe or psychotic depression than older female patients. Previously, it has been found that longer hospital episode associates with patient functional incapacity and negative depressive symptoms, such as anhedonia, loss of interest and lack of motivation and motor retardation [16].

In addition, the average length of inpatient episode in affective disorders was longer in men, especially middle-old age group, compared to same age women. Bergdahl et al. [26] found that depression in old age differs between genders. According to their findings, men had more motivation-related symptoms and agitation, while women had more often mood-related symptoms. Feasible explanations for longer inpatient episodes include health problems, chronic disease

and widowhood, which have previously been associated with depression in males [26]. Further, according to the previous review study by Kessing [28], it has been suggested that some forms of depressive illness, for example, depression before young-old age (before age 65 years) and recurrent depression, may constitute long-term risk factors for development of dementia, whereas the onset of more recent depressive symptoms may reflect a prodromal phase of dementia. Still, it is not clear whether specific subtypes of depression correspond to specific types of dementia.

Future research examining more detailed sociodemographic and clinical factors, which are likely associated with length of inpatient episodes among patients with affective disorders is called for.

Psychotic disorders formed over one-fourth of all diagnoses in inpatient episodes. We found that the average length of hospital treatment in psychotic disorders was longest in middle-olds (75-84 years old patients) in both genders. In a review article, Gopalakrishna et al. [1] showed that psychotic and affective disorders, as well as patient age, was associated with longer length of stay in hospital. Explanations for longer inpatient episodes among elderly patients may be that patients have less social support, are living alone or have poorer overall health [29].

Our study indicates that inpatient episodes with psychotic disorders were more common among oldest-old men than women. Henderson et al. [30] established in their population-based study that risk factors for psychotic symptoms in old age are male gender and cognitive impairment. Previously, it had been established that psychotic symptoms in old people may be a part of prodromal symptoms of dementia [31]. Some estimates suggest that up to 60% of all psychotic episodes in the elderly begin due to onset of a secondary medical condition [13]. Some conditions that may lead to secondary psychotic episodes include metabolic, infectious, neurological and endocrine diseases. This would suggest to diagnose for psychotic symptoms at an early stage, as it has been found to affect several outcomes, such as mortality and somatic disorders [7].

Anxiety disorders formed 10% of psychiatric diagnoses in inpatient episodes in our study. Further, inpatient episodes due to anxiety disorders were twice that of middle-old and oldest-old women than men in the same age groups. Our findings are in line with results from the Berlin Aging study [32] which established that anxiety disorders were slightly more common among females than males among 70-84 years old subjects. They also found that anxiety disorders do not increase with age. One possible explanation for our findings

is that we focused only on main psychiatric diagnoses. In a previous study [2], anxiety feelings associated with females and psychiatric disorders, like comorbid anxiety disorders and depression as well as with dementia. Furthermore, anxiety may also associate with several factors, like social loneliness or somatic comorbidity [32]. Anxiety may be a premorbid symptom of even Parkinson's disease, which is a common progressive neurodegenerative disorder among older adults [33]. Anxiety disorders have been found to have an adverse impact on cognitive functioning ([34], and thus they may weaken performance at home. It has been argued that anxiety among old people is more common than depression, but less studied [34]. Our finding of the association of anxiety disorders and oldest-old patients, however, warrants further studies in large samples of elderly patients from different treatment settings.

In our study, the average length of stay of hospital episode was longer among anxiety disorders with oldest-old patients compared to younger patients. Earlier studies have suggested that anxiety feelings may be associated with depressive disorder or dementia as well as with decreased health and stressful life events, which may be more common in older subjects than in younger [2]. Though anxiety disorders are infrequent in the elderly, they may, however, increase the need for health and social services [35]. In conclusion, our study emphasizes the importance of evaluating the anxiety disorders of oldest-old people, especially those with cognitive impairment or somatic complaints.

The study sample consisted of patients in psychogeriatric ward, and therefore it is obvious that the number of somatic diagnoses marked as main diagnosis was low. Nevertheless, elderly patients may have somatic disorders at the same time as psychiatric disorders. Our focus in this study was the main diagnoses of inpatient episodes and therefore psychiatric and somatic comorbidity was beyond the focus of our analysis. Inpatient episodes and average inpatient days per patient have remained stable with little fluctuation year by year. These differences may be explained by ward closures during 2012-2018, with more patients treated in the ward during years without closure after year 2019.

As is well known, the length of stay of hospital episode may be associated with various demographic, treatment-related and diagnosis-related variables [1]. In order to get a deeper understanding of factors related to psychogeriatric inpatients, further studies by larger databases than ours are called for to investigate the relationship between psychiatric and somatic morbidity in old age.

In terms of our time series data, the Covid-19 pandemic had an impact on the Finnish healthcare system during 2020-2021 [36]. Our study revealed that there was an increase in the proportion of oldest-old inpatient group (aged over 85) in 2020, with a decline in 2021 to near pre-pandemic levels. Notably, in 2021 there occurred a relative increase in proportion of episodes for young-olds. Whether these changes were a result of the pandemic remains an important question for further research.

During the years 2012-2018, the length of closure of the psychogeriatric ward varied from eight to 66 days, mainly because of lack of labour resources due to vacations. We believe, however, that these ward closures may have had only minimal, if any, impact on our main results regarding characteristics of psychogeriatric patients. Unfortunately, no data was available for evaluating generally the impact of ward closure days on the patients needing psychiatric care in the Oulu University Hospital.

Although the psychogeriatric ward is a small unit located in Oulu University Hospital, providing specialized level healthcare, it has several roles in mental health services for the elderly population in the wellbeing services counties of North Ostrobothnia (Pohde) and Lapland (Lapha) in Northern Finland. Firstly, it has a special role for diagnosing and taking care of the most challenging elderly inpatients needing specialized level psychiatric care. Secondly, it has an essential consultation role with geriatric and other healthcare units of the two northernmost wellbeing service counties of Finland. Thirdly, the psychogeriatric unit has an important role in educating trainers in psychiatry and geriatrics in northern Finland.

STRENGTHS

The most important strength of our study is register-based data giving us access to comprehensive follow-up data of all inpatient episodes in the psychogeriatric ward during 2012-2021. Another strength is that all psychiatric diagnoses were based on clinicians' judgement. Diagnoses were analysed using ICD-10 diagnostic criteria, which means our findings can easily be compared to international studies. Studies based on Finnish healthcare register data have been shown to be satisfactory for research purposes [37,38].

LIMITATIONS

Our study has several limitations. We had no access to hospital case notes. Thus, this study does not include information on patients' comorbid psychiatric and somatic

diagnoses, medication or methods of treatment and other medically relevant data. Further studies on psychiatric comorbidity and medication among elderly inpatients are, therefore, required. One limitation was that the impact of involuntary stays versus voluntary stays on the length of hospitalization could not be analysed because of lack of that information. Finally, our study sample consisted of severe, hospitalized manifestations of the psychiatric disorders. Unfortunately, in this study we had no access to the register data of other psychiatric and geriatric healthcare wards located in the catchment area of Oulu University Hospital. It is likely that the age and diagnostic distribution in these units is different than in our study, which utilized the specialized level register data of psychogeriatric patients. This limits the ability to generalize our findings to all old people with less severe mental health problems.

CONCLUSIONS

The findings of our register-based study of hospitalized psychogeriatric inpatients brings a novel insight into current psychiatric inpatient care involving elderly patients. The ageing of the population has had an impact on many fields of society, including healthcare. Our study also illustrates the need for better means to identify those different aged elderly patients in need of psychiatric care. These elderly patient groups may need different mental health services in young-old age than in middle-old age. Elderly subjects are known to highly benefit from timely treatment. Longer delay in appropriate care can lead to greater loss of level of daily functioning and have adverse effects on the quality of life of the elderly. Our results could be used when planning mental health services for the elderly population in wellbeing service counties, as well as in the allocation of healthcare resources.

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References

1. Gopalakrishna G, Ithman M, Malwitz K. Predictors of length of stay in a psychiatric hospital. *Int J Psychiatry Clin Pract* 2015;19:239-245.
2. Forsell Y, Winblad B. Feelings of anxiety and associated variables in a very elderly population. *Int J Geriatric Psychiatry* 1998;13:454-458.
3. Djernes JK. Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatr Scand* 2006;113(5):372-387.
4. Almeida OP, Hankey GJ, Yeap BB, Golledge J, Norman PE, Flicker L. Mortality among people with severe mental disorders who reach old age: A longitudinal study of a community-representative sample of 37892 men. *PLOS ONE* 2014; 9(10):3111882.
5. Gálvez V, Ho KA, Alonzo A, Martin D, George D, Loo CK. Neuromodulation therapies for geriatric depression. *Curr Psychiatry Rep* 2015;17:59.
6. Colijn MA, Nitta BH, Grossberg GT. Psychosis in later life: A review and update. *Harv Rev Psychiatry* 2015;23:354-67.
7. Skoog I. Psychiatric epidemiology of old age: the H70 study – the NAPE Lecture 2003. *Acta Psychiatr Scand* 2004;109:4-18.
8. Skoog I. Psychiatric disorders in the elderly. *Can J Psychiatry* 2011;56:387–397.
9. Sjöberg L, Karlsson B, Atti A-R, Skoog I, Fratiglioni L, Wang H-X. Prevalence of depression: Comparisons of different depression definitions in population-based samples of older adults. *J Affect Disord* 2017;(221):123-131.
10. Kok RM, Reynolds CF. Management of depression in older adults: A review. *JAMA* 2017;317:2114-2122.
11. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety disorders in older adults: a comprehensive review. *Depress Anxiety* 2010;27:190-211.
12. Bakkane Bendixen A, Engedal K. Anxiety among older psychiatric patients: a hidden comorbidity? *Aging Ment Health* 2016;20(11):1131-1138.
13. Reinhardt MM, Cohen CI. Late-life psychosis: diagnosis and treatment. *Curr Psychiatry Rep* 2015;17:1.
14. Colijn MA, Nitta BH, Grossberg GT. Psychosis in later life: A review and update. *Harv Rev Psychiatry* 2015;23(5):354-367.
15. Hiltunen P 1999. Psychiatric consultation in general hospital in Finland. Referrals under and over 65 to liaison psychiatrists (Doctoral dissertation, University of Oulu). *Acta Universitatis Ouluensis D, Medica* 1999;567.
16. Ismail Z, Arenovich T, Grieve C, Sajeev G, Mamo DC et al. Predicting hospital length of stay for geriatric patients with mood disorders. *Can J Psychiatry* 2012;57(11):696-703.
17. OECD. Elderly population (Indicator). 2022. doi 10.1787/8d805ea1-en (Accessed on 02 November 2022).
18. The Wellbeing Services County of North Ostrobothnia. <https://Pohde.fi>.

19. De Rango F, Montesanto A, Berardelli M, Mazzei B, Mari V, et al. To grow old in Southern Italy: A comprehensive description of the old and oldest old in Calabria. *Gerontology* 2011;57:327-334.
20. Erber JT. *Aging and older adulthood*. 4th ed. Wiley Blackwell 2019.
21. Oulu University Hospital, division of psychiatry. Annual reports on ward of geriatric psychiatry 2012-2021.
22. Tautiluokitus ICD-10. Sosiaali- ja terveystalouden tutkimus- ja kehittämiskeskus. 1995. <https://urn.fi/URN:NBN:fi-fe201205085423>.
23. Tilastokeskus, Statistics Finland 2022. www.stat.fi/tietokantataulukot.
24. Heikkinen R-L, Kauppinen M. Depressive symptoms in late life: a 10-year follow-up. *Arch Gerontology and Geriatrics* 2004;38:239-250.
25. Partent V, Ludwig-Béal S, Sordet-Guépét H, Popitéan L, Camus A et al. Prolonged stays in hospital acute geriatric care units: Identification and analysis of causes. *Geriatr Psychol Neuropsychiatr Vieil* 2016;1:14(2):135-141.
26. Bergdahl E, Allard P, Alex L, Lundman B, Gustafson Y. Gender differences among very old. *Int Psychogeriatrics* 2007;19(6):1125-1140.
27. Choi S, Rozario P, Morrow-Howell N, Proctor E. Elders with first psychiatric hospitalization for depression. *Int J Geriatr Psychiatry* 2009;24(1):33-40.
28. Kessing LV. Depression and the risk for dementia. *Curr Opin Psychiatry* 2012;25:457-461.
29. Pertile R, Donisi V, Grigoletti L, Angelozzi A, Zamengo G et al. DRGs and other patient-, service- and area-level factors influencing length of stay in acute psychiatric wards: the Veneto. Venetian experience. *Soc Psychiatry Psychiatric Epidemiol* 2010;1-10.
30. Henderson AS, Korten AE, Levings C, Jorm AF, Christensen H et al. Psychotic symptoms in the elderly: A prospective study in a population sample. *Int J Geriatr Psychiatry* 1998;13:484-492.
31. Östling S, Bäckman K, Sigström R, Skoog I. Is the prevalence of psychosis in the very old decreasing? A comparison of 85-year-olds born 22 years apart. *Int J Geriatr Psychiatry* 2019;34:1776-1783.
32. Scahub RT, Linden M. Anxiety and anxiety disorders in the old and very old--results from the Berlin Aging Study (BASE). *Compr Psychiatry* 2000;41 (2 Suppl 1):48-54.
33. Beitz JM. Parkinson's disease: a review. *Frontiers in Bioscience* 2014; S6:56-74.
34. Blau SL, Marinho V. Anxiety disorders in old age. *Curr Opin Psychiatry* 2012;25:462-467.
35. Lloyd KR, Jenkins R, Mann A. Long term outcome of patients with neurotic illness in medical practice. *Br Med J* 1996;313:26-28.
36. Summanen M, Kosunen M, Kainu V, Cansel A, Niskanen S et al. COVID-19 hospitalisations and all-cause mortality by risk group in Finland. *PLOS One* 2023; 18(5): e0286142.

37. Miettunen J, Suvisaari J, Haukka J, Isohanni M. Use of register data for psychiatric epidemiology in the Nordic countries: Textbook of psychiatric epidemiology. In: Tsuang M, Tohen M, Jones P (ed) Textbook of psychiatric epidemiology. Wiley-Balckwell 2011. pp 117-131.
38. Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. Scand J Publ Health 2012;40(6):505-515.



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DISORGANIZED THINKING AND EMOTIONAL POVERTY ARE PRIMARY CLINICAL PREDICTORS OF FUNCTIONING IN PSYCHOSES. REANALYSIS OF THE TURKU EARLY PSYCHOSIS STUDY DATA

ABSTRACT

Background: The functional outcomes of patients with a psychotic disorder have been associated with several overlapping clinical, neuropsychological and developmental factors.

Aim: In a prospective study, we aimed to predict functional outcomes in patients with first-episode psychosis or clinically high risk for psychosis by sociodemographic, clinical, neuropsychological and premorbid factors and follow-up symptomatology.

Methods: Altogether, 130 first-episode psychosis and 60 clinical high-risk patients were recruited, and their functioning was assessed at baseline and at 9- and 18-month follow-ups. The total follow-up functioning was predicted by baseline characteristics and factorized dimensions of baseline clinical symptoms, premorbid adjustment, childhood adversities, neuropsychological tests and follow-up symptoms.

Results: Emotional Poverty and Disorganized Thinking, premorbid Sociability and Scholastic Performance, social support, baseline functioning, follow-up Depression/Anxiety and Psychoticism correlated significantly with follow-up functioning. In the regression model, follow-up functioning was significantly associated with Sociability and Scholastic Performance, Disorganized Thinking, work and marital status in the entire sample and in psychotic patients separately. In clinical high-risk patients, Emotional Poverty and follow-up depression/anxiety symptomatology were significantly associated with poor follow-up functioning. The effects of Sociability and School Performance on follow-up functioning were mediated via Emotional Poverty in both patient groups.

Conclusion: In psychotic patients, poor premorbid adjustment, disorganized thinking, poor baseline work status and being single predicted poor follow-up functioning. The effect of premorbid adjustment on follow-up functioning was partly mediated via emotional poverty. In clinical high-risk patients, basic disturbances were affective disorders, and attenuated psychotic symptoms represented their severity.

KEYWORDS: FUNCTIONAL OUTCOME, PSYCHOSIS, CLINICAL HIGH RISK FOR PSYCHOSIS, PREMORBD PSYCHOSOCIAL ADJUSTMENT, DISORGANIZED SYMPTOMS, EMOTIONAL POVERTY, NEGATIVE SYMPTOMS, EMPLOYMENT SITUATION, MARITAL STATUS

INTRODUCTION

PSYCHOSIS

According to Emil Kraepelin [1], classification of mental diseases should be based on illness course and outcome. Using follow-up observations of hospitalized patients, he described dementia praecox with poor and manic-depressive psychoses with good course. Characteristic clinical features of dementia praecox were disturbed courses of thought (Gedankengang), emotional dullness, apathy, lack of interest and volition, diminished work capacity and overall lack of emotional activity. Eugen Bleuler [2] emphasized the need for early diagnosis and the significance of illness symptoms and replaced the dementia praecox with a group of schizophrenic patients with a better but more variable course. In the illness picture, loosening of associations, found in all patients, was primary and behind the fundamental symptoms: formal thought disorders (typically incoherent train of thought) and affect disturbances (typically flattening of affects). Other fundamental symptoms were ambivalence and autism, while delusions, hallucinations and catatonic symptoms were regarded as accessory symptoms [2].

Schneider [3] introduced the concept of first-rank symptoms, which were reliably detectable in all cultures and frequently seen in patients with schizophrenia but also in other severe psychiatric disorders, even in neurological disorders. In a follow-up study, first-rank symptoms were not associated with poor prognosis in schizophrenia [4].

Later, the group of schizophrenias was divided into Kraepelinian nuclear schizophrenia with poor prognosis and schizophreniform psychoses with good prognosis [5] and process/reactive schizophrenia with poor/good premorbid development and poor/good prognosis [6]. In two 7½-year follow-up studies of first-time hospitalized patients, patients with nuclear schizophrenia had poorer outcomes than patients with schizophreniform psychoses [7-8].

Strauss et al. [9] proposed a distinction between positive and negative symptoms. These symptom categories, accepted by other researchers [10], have been adopted in various symptom classifications. In addition to negative symptoms, poor premorbid psychosocial development, educational and work achievement, male gender, single marital status and lack of interpersonal networks have been associated with poor illness course and functional outcomes in patients with schizophrenia [7,8,11,12,13,14,15,16,17,18,19,20,21,22,23,24].

Patients with schizophrenia have also shown cognitive deficits, including worse intellectual function, learning and memory, attention, working memory, language, executive function and social cognition [25,26,27,28,29,30]. However, baseline neurocognitive impairments have not been associated with clinical outcome [31]. Additionally, childhood adversities have been associated with psychotic disorders [32,33,34] and with persistence of psychotic symptoms and poor outcomes [35,36].

CLINICAL HIGH RISK FOR PSYCHOSIS (CHR)

As early as 1887, Emil Kraepelin [37] described that mental illness (Geisteskrankheit) mostly begins gradually; a sudden beginning is mostly a reaction to external causes. Almost regularly, small changes in emotional life (Gefülsleben) are the first signs, but it may take weeks, months or even years before the onset of a mental illness. This prodromal stage (Stadium der Prodrome) may appear as emotional irritation, restlessness or depressiveness. When the stage of uncharacteristic prodromal disturbances retreats, the characteristic initial symptoms (Initialsymptome) of psychosis become visible. Bleuler's [2] description of "latent schizophrenia" represents a prodromal disturbance without characteristic symptoms of schizophrenia or its 'forme fruste' [38].

Hoch and Polatin [39] described pseudoneurotic forms of schizophrenia with brief and limited psychotic episodes (micropsychoses) and found that 20% of these patients became schizophrenic [40]. In two 8-year follow-up studies, 15.4% of patients with pseudoneurotic schizophrenia became psychotic. Compared with patients with nuclear schizophrenia and schizophreniform psychoses, their outcome was better [7-8].

In the 1960s, Huber [41] described anomalous subjective experiences (basic symptoms) that can develop into psychosis (prodromes) or resolve spontaneously (outpost syndromes) [41,42,43]. Based on these observations, instruments Bonn Scale for the Assessment of Basic Symptoms (BSABS) and Schizophrenia Proneness Instrument, Adult Version (SPI-A) [44,45] were developed for detecting individuals at high risk for psychosis. Using a combination of positive symptoms, changes in functioning and family history, two other instruments, the Comprehensive Assessment of At-Risk Mental States (CAARMS) [46,47,48] and Structured Interview for Prodromal Syndromes/Scale of Prodromal Symptoms (SIPS/SOPS) [49,50], have been developed and widely used.

Clinical High Risk for Psychosis (CHR) patients are characterized by many clinical disorders, including substance use, affective disorders, suicidal ideation and self-harm, and have impairments in work or in educational and social functioning [51]. In patients with CHR, e.g., long duration of prodromal symptoms, positive symptoms, bizarre thinking, schizotypal personality, substance abuse, low education, depression, disorganization, neurocognitive deficits and poor psychosocial development have been associated with onset of psychosis [52,53,54,55,56,57,58]. According to a systematic review, negative symptoms and disorganized symptoms and cognitive deficits predate frank psychotic symptoms and are risk factors for poor functioning [59].

In CHR patients, impaired emotion recognition and processing speed and deficits in motor speed, verbal memory, verbal learning, verbal fluency and executive function have been associated with the onset of psychosis and poor functioning [58,60,61,62,64]. Additionally, patients with CHR report high levels of childhood adversity [65,66]; this adversity may predict depression, poor social functioning and suicidal thinking [66,67,68].

In terms of premorbid functioning, CHR subjects have not differed from patients with first-episode psychosis or multi-episode schizophrenia [69]. In outcome studies of CHR patients, premorbid psychosocial adjustment, baseline negative symptoms and poor employment/study situations have predicted poor functional outcomes at follow-up [63,64,70,71].

In our previous study, we found that sum scores of premorbid adjustment, assessed by the Premorbid Adjustment Scale (PAS) [72], and sum scores of disorganized symptoms of the Structured Interview for Prodromal Syndromes (SIPS) [49, 73], and one of several neuropsychological (NEUPSY) tests were the major predictors of follow-up functioning in patients with clinical or subclinical psychotic disorders [74,75]. However, PAS and SIPS scores and NEUPSY tests used in analyses are combinations of heterogeneous items. Therefore, in order to reduce heterogeneity of these measurements we factorized PAS, SIPS and NEUPSY items and follow-up symptoms and used these factor dimensions in our analyses. Using more homogeneous explanatory factors, we expected that the practitioner planning interventions for psychotic patients can also receive a more concise and understandable view of the factors predicting patient's functional outcome.

In the present study, our first aim was to predict 9- to 18-month functional outcomes with premorbid, baseline and follow-up factor dimensions in patients with first-episode

psychosis (FEP) and clinical high risk for psychosis (CHR). We proposed that PAS can express the effects of very early, like genetic and external, factors that can modulate the clinical factors available at the moment when the clinicians first time meet psychotic patients and concurrently associate with functional outcome. Thus, our second aim was to investigate whether the effect of PAS on follow-up functioning is mediated via baseline clinical factor dimensions. The 18-month follow-up is justified because interventions, aimed at improving both clinical and functional outcomes over longer time periods, should be performed during this critical period.

METHODS

The investigations of the Turku Early Psychosis Study (TEPS) study programme were carried out in accordance with the latest version of the Declaration of Helsinki, and the study design and protocols were approved by the ethical committee of the Turku University Hospital. Written informed consent from participants was obtained after the procedure had been fully explained to them.

SAMPLE AND EXAMINATIONS

The TEPS is a prospective study in which the sample and examinations were described in detail in our previous article [74-75]. Altogether, 130 FEP and 60 CHR patients were recruited from the services of the Turku University Hospital District in Finland between October 2011 and December 2017.

FEP was defined by the Structured Clinical Interview for DSM-IV (SCID-I) criteria and included schizophrenia, delusional and bipolar psychoses, acute and transient psychoses and other psychoses. CHR was defined by the ultra-high risk (UHR) criteria: Attenuated Psychotic Symptoms (APS), Brief Limited Psychotic Symptoms (BLIPS) and genetic risk and reduction of function (GRD) assessed by the 3.0/5.0 version of the Structured Interview for Prodromal Syndromes (SIPS/SOPS) including the Global Assessment of Functioning (GAF) scale [49,73].

At baseline, information on socioeconomic background, premorbid adjustment (PAS) [72], SIPS symptoms (SIPS/SOPS), including GAF [49,73] and Axis I diagnosis (the Structured Clinical Interview for DSM-IV, Axis I) [76] were received in interviews. Neuropsychological tests (NEUPSY) were obtained from 119 (92%) out of 130 FEP and from 54

(90%) out of 60 CHR patients when the patients recovered from their acute psychosis.

Self-rating questionnaires on adverse and traumatic experiences in childhood (the Trauma and Distress Scale (TADS) [77,78]) and social support (Perceived Social Support Scale-Revised (PSSS-R) [79]) received from close confidants were also obtained. The PSSS-R includes 12 questions on social support received. The sum score (range 0-48) was used as an indicator of social support. Details of PAS, SIPS/SOPS, TADS and NEUPSY and their factor analyses are described in the Supplementary Material.

All subjects examined at baseline were invited to follow-up studies 9 (T1) and 18 (T2) months after the baseline examination. For this outcome study, GAF at baseline (GAFT0) and at the follow-up points (GAFT1 and GAFT2) and occurrence of psychosis (yes/no), depression (yes/no) and anxiety (yes/no) symptoms at the follow-up points (T1 and T2) were recorded. Due to follow-up dropouts, information regarding both functioning (GAF) and psychiatric symptoms was supplemented by scrutinizing patients' medical case notes and by telephone interviews with patients and/or their relatives and/or their doctors. GAF and psychosis, depression and anxiety symptoms were obtained for 190 (T0), 189 (T1) and 188 (T2) patients. Thus, there was one dropout at T1 and two dropouts at T2.

STATISTICAL ANALYSES

First, distributions of background factors were cross-tabulated, and means and SD of GAF, SIPS, TADS, PSSS-R, PAS and NEUPSY scores were calculated by diagnostic groups and tested by Chi-square tests and analyses of variance (ANOVAs). The sum of GAFT1 and GAFT2 was calculated, and this sum score was used to describe follow-up functioning (F-GAF).

Principal component factor analyses with varimax rotation were calculated from PAS, SIPS, TADS and NEUPSY items and follow-up symptoms, and the factors received were interpreted (*Supplementary Tables 2-6*). Means of factor dimension scores were calculated by diagnostic groups, and differences were tested with ANOVAs. Pearson correlation coefficients were calculated for the PAS, SIPS, TADS and NEUPSY dimensions and PSSS-R scores.

In multivariate analyses, F-GAF was predicted by background characteristics, PAS, SIPS, TADS and NEUPSY dimensions, and social support scores in linear regression analyses. Thereafter, follow-up psychiatric symptom dimensions were also included in the regression analyses.

Finally, a PROCESS macro in SPSS (model template 4) created by Hayes [80] was used. In cross-sectional samples, this macro tests the direct and indirect effects of an independent variable (X) on a dependent variable (Y) while modelling a process in which X affects a mediator (M), which in turn affects Y. The models tested the effect of X (PAS) on Y (F-GAF) with mediators (SIPS, TADS and NEUPSY dimensions and PSSS-R scores). Five thousand bootstrap samples and 95% confidence intervals were used for all analyses. The PROCESS macro was developed for cross-sectional analyses, but in the present study, it was applied in a prospective design.

Analyses were performed for all study subjects and in sensitivity analyses for FEP and CHR patients separately. Data were analysed using the Statistical Programme for the Social Sciences (SPSS) v26.0, and p values <0.05 were considered statistically significant.

RESULTS

BASELINE ANALYSES

In FEP patients, 33.8% had affective and 66.2% had non-affective psychosis. A majority of the CHR patients suffered from depression (56.7%) and anxiety (26.7%) disorders. The FEP patients reported more social support and, by diagnostic definition, more SIPS-positive symptoms. Otherwise, there was no difference in background characteristics, SIPS symptoms, TADS or PAS scores. At baseline, GAF was lower in FEP patients than in CHR patients. During follow-up, GAF in the FEP ($p<0.001$) and CHR ($p=0.007$) groups improved. However, at follow-up, there was no difference in F-GAF between the diagnostic groups (*Table 1*).

Table 1. Sociodemographic background and baseline characteristics of the Turku Early Psychosis Study (TEPS) sample

	FEP	CHR	All	p
Gender	n=130	n=60	n=190	0.336
Male	56.2	51.7	54.7	
Female	43.8	48.3	45.3	
Age (years)	n=130	n=60	n=190	0.124
18-23	37.7	53.3	42.6	
24-29	33.1	23.3	30.0	
30-49	29.2	23.3	27.4	
mean (SD)	26.5(5.9)	25.0(6.2)	26.1(6.0)	0.111
Marital status	n=130	n=60	n=190	0.999
Single	72.3	71.7	72.1	
Ever married/divorced	27.7	28.3	27.9	
Basic education	n=130	n=60	n=190	0.347
Elementary school or less	40.0	41.7	40.5	
High school	13.8	6.7	11.6	
College	46.2	51.7	47.9	
Professional education	n=130	n=60	n=190	0.254
None	43.8	48.3	45.3	
Vocational school	41.5	43.3	42.1	
University	14.6	8.3	12.6	
Years of education; mean (SD)	13.8(3.1)	13.2(2.9)	13.6(3.0)	0.207



	FEP	CHR	All	p
Employment situation	n=130	n=60	n=190	0.574
Employed	60.0	58.3	59.5	
Unemployed	19.2	30.0	22.6	
Sick leave	10.8	6.7	9.5	
Temporary pension	10.0	5.0	8.4	
Social support	n=104	n=48	n=152	
mean, SD	31.4(11.5)	27.4(10.7)	30.2(11.4)	0.046
SCID Diagnosis (%)	n=130	n=60	n=190	<0.001
None	0.0	8.3	2.6	
Bipolar	16.9	3.3	12.6	
Depression	16.9	56.7	29.5	
Non-affective Psychosis	66.2	5.0	46.8	
Anxiety	0.0	26.7	8.4	
SIPS symptoms	n=125	n=60	n=185	
Positive (0-30)	16.5(5.3)	10.6(5.9)	14.6(5.6)	<0.001
Negative (0-30)	11.0(7.2)	11.4(6.5)	11.1(6.9)	0.760
Disorganized (0-24)	5.4(4.0)	4.9(3.4)	5.3(3.9)	0.325
General (0-24)	6.8(4.5)	7.7(3.3)	7.1(4.2)	0.162
TADS mean (SD)	n=107	n=48	n=155	
EmoAb (1-5)	4.7(4.3)	5.3(4.4)	4.9(4.3)	0.449
PhyAb (1-5)	1.7(2.1)	1.8(2.6)	1.8(2.2)	0.831



	FEP	CHR	All	p
SexAb (1-5)	1.2(3.1)	0.6(1.6)	1.0(2.7)	0.242
EmoNeg (1-5)	6.8(5.0)	7.5(5.1)	7.0(5.0)	0.469
PhyNeg (1-5)	3.4(2.8)	3.3(3.1)	3.4(2.9)	0.831
PAS mean (SD)	n=124	n=57	n=181	
-11 years (0-24)	6.2(3.6)	6.8(3.3)	6.4(3.5)	0.278
12-15 years (0-30)	10.1(5.2)	10.8(4.9)	10.3(5.1)	0.427
16-18 years (0-30)	10.9(5.6)	10.9(5.9)	10.9(5.6)	0.998

FEP = First-episode psychosis; CHR = clinical high-risk to psychosis; EmoAb = Emotional abuse; PhyAb = Physical abuse; SexAb = Sexual abuse; EmoNeg = Emotional neglect; PhyNeg = Physical neglect; PAS = Premorbid adjustment

In neurocognitive tests of attention, speed of processing, verbal learning and visual learning, the CHR patients performed better than FEP patients (*Supplementary Table 1*). In other tests, there was no difference between FEP and CHR patients.

FACTOR ANALYSES ON SIPS SYMPTOMS, NEUROPSYCHOLOGICAL TEST PARAMETERS, TADS DOMAINS AND FOLLOW-UP SYMPTOMS

Factor analysis of SIPS items yielded four dimensions: emotional distress, emotional poverty, disorganized thinking and delusions/hallucinations (*Supplementary Table 2*). Social anhedonia/withdrawal and avolition loaded on the Emotional Distress and Emotional Poverty dimensions, indicating some overlap and decrease in mood and emotional response in these dimensions. Odd behaviour/appearance loaded on Emotional Poverty and Disorganized Thinking dimensions describing the inability to take care of appearance and to behave coherently.

Factor analyses for NEUPSY yielded four factor dimensions: executive functions, cognitive performance, perceptual disturbances and verbal skills. For TADS domain there was one factor, childhood trauma. For PAS items, there were two factors, sociability and school performance. For follow-up symptoms, there were two factor dimensions,

depression/anxiety and psychoticism (*Supplementary Tables 3-6*).

In CHR patients, Emotional Distress, Cognitive Performance and Depression/Anxiety dimension scores were higher than in FEP patients, whereas in Disorganized Thinking and Delusional/Hallucinatory and Psychoticism dimensions, the situation was reversed (*Supplementary Figure 1*).

The employment situation, GAFT0, SIPS dimensions Emotional Poverty and Disorganized Thinking, PAS Sociability and School Performance, social support, and follow-up Depression/Anxiety and Psychoticism correlated significantly with F-GAF. It was notable that the NEUPSY and Childhood Trauma had no significant correlation with the F-GAF (*Table 2*).

Table 2. Correlation between baseline functioning (GAFT0), follow-up functioning (F-GAF) scores, Structured Interview for Prodromal Syndromes (SIPS), neuropsychological tests (NEUPSY), Premorbid Adjustment Scale (PAS), Trauma and Distress Scale (TADS) dimensions, Perceived Social Support Scale-Revised (PSSS-R) scores and follow-up symptom dimensions

	0	1.	2.	3.	4.	5.	6.	7.
0. GAFT0	1	.438**	-.220**	-.216**	-.307**	-.159*	-.031	.222**
1. F-GAF (GAFT1+GAFT2)	.438**	1	-.119	-.368**	-.240**	-.003	.083	.131
SIPS dimensions								
2. Distress	-.220**	-.119	1	.000	.000	.000	.026	-.009
3. Emotional Poverty	-.216**	-.368**	.000	1	.000	.000	-.162*	-.246**
4. Disorganized Thinking	-.307**	-.240**	.000	.000	1	.000	-.006	-.049
5. Delusory/Hallucinatory	-.159*	-.003	.000	.000	.000	1	.045	-.237**
NEUPSY dimensions								
6. Executive Functions	-.031	.083	.026	-.162*	-.006	.045	1	.000
7. Cognitive Performance	.222**	.131	-.009	-.246**	-.049	-.237**	.000	1
8. Perceptual Disturbances	.223**	.134	-.107	-.135	-.205**	-.009	.000	.000
9. Verbal Skills	.084	.141	-.232**	-.143	-.001	.029	.000	.000
PAS dimensions								
10. Sociability	-.222**	-.278**	.296**	.385**	.076	.034	-.059	-.063
11. Scholastic Performance	-.079	-.354**	.028	.373**	.001	-.024	-.146	-.333**
TADS domain dimension								
12. Childhood Trauma	.063	-.117	.115	.171*	-.091	.050	.034	.024
PSSS-R scores								
13. Social support	.124	.243**	-.331**	-.304**	.077	-.025	-.091	.113
Follow-up symptom dimensions								
14. Depression/Anxiety	-.138	-.402**	.186*	.098	-.084	-.152*	-.150*	.004
15. Psychoticism	-.197**	-.569**	-.110	.138	.217**	.188*	.044	-.159*



	8.	9.	10.	11.	12.	13.	14.	15.
0. GAFT0	.223**	.084	-.222**	-.079	.063	.124	-.138	-.197**
1. F-GAF (GAFT1+GAFT2)	.134	.141	-.278**	-.354**	-.117	.243**	-.402**	-.569**
SIPS dimensions								
2. Distress	-.107	-.232**	.296**	.028	.115	-.331**	.186*	-.110
3. Emotional Poverty	-.135	-.143	.385**	.373**	.171*	-.304**	.098	.138
4. Disorganized Thinking	-.205**	-.001	.076	.001	-.091	.077	-.084	.217**
5. Delusionary/Hallucinatory	-.009	.029	.034	-.024	.050	-.025	-.152*	.188*
NEUPSY dimensions								
6. Executive Functions	.000	.000	-.059	-.146	.034	-.091	-.150*	.044
7. Cognitive Performance	.000	.000	-.063	-.333**	.024	.113	.004	-.159*
8. Perceptual Disturbances	1	.000	-.027	-.066	-.021	-.011	-.112	-.022
9. Verbal Skills	.000	1	-.037	-.327**	.120	.072	.021	.037
PAS dimensions								
10. Sociability	-.027	-.037	1	.000	.238**	-.459**	.121	.031
11. Scholastic Performance	-.066	-.327**	.000	1	.059	-.156	.216**	.164*
TADS domain dimension								
12. Childhood Trauma	-.021	.120	.238**	.059	1	-.354**	.183*	-.043
PSSS-R scores								
13. Social support	-.011	.072	-.459**	-.156	-.354**	1	-.152	.011
Follow-up symptom dimensions								
14. Depression/Anxiety	-.112	.021	.121	.216**	.183*	-.152	1	.000
15. Psychoticism	-.022	-.037	.031	.164*	-.043	.011	.000	1

** . Correlation is significant at the 0.01 level (2-tailed)

* . Correlation is significant at the 0.05 level (2-tailed)

MULTIVARIATE PREDICTION OF FOLLOW-UP FUNCTIONING

In linear regression analysis, baseline marital status (single), poor employment situation, Disorganized Thinking, difficulties in premorbid Sociability and School Performance associated with poor F-GAF (*Table 3 A*). In FEP patients, the associations were the same as in the entire sample (*Table 3 B*). In CHR patients, only Emotional Poverty significantly associated with F-GAF (*Table 3 C*).

Table 3. Regression analyses for follow-up functioning in the total sample (A.) and in the patients with first-episode psychosis (B. FEP) and with clinical high risk for psychosis (C. CHR) separately

A. TOTAL SAMPLE

R² 0.342	B	p	CI95%	
Marital status (single)	10.047	0.038	0.588	19.507
Employment situation	-8.782	<0.001	-13.186	-4.377
Disorganized thinking	-7.492	<0.001	-11.608	-3.376
Sociability	-6.122	0.006	-10.472	-1.772
Scholastic Performance	-11.498	<0.001	-15.666	-7.330

B. FEP

R² 0.400	B	p	CI95%	
Marital status (single)	15.519	0.011	3.622	27.416
Employment situation	-8.391	0.002	-13.711	-3.070
Disorganized thinking	-8.351	0.001	-13.062	-3.640
Sociability	-5.601	0.044	-11.052	-.151
Scholastic Performance	-13.066	<0.001	-18.287	-7.845

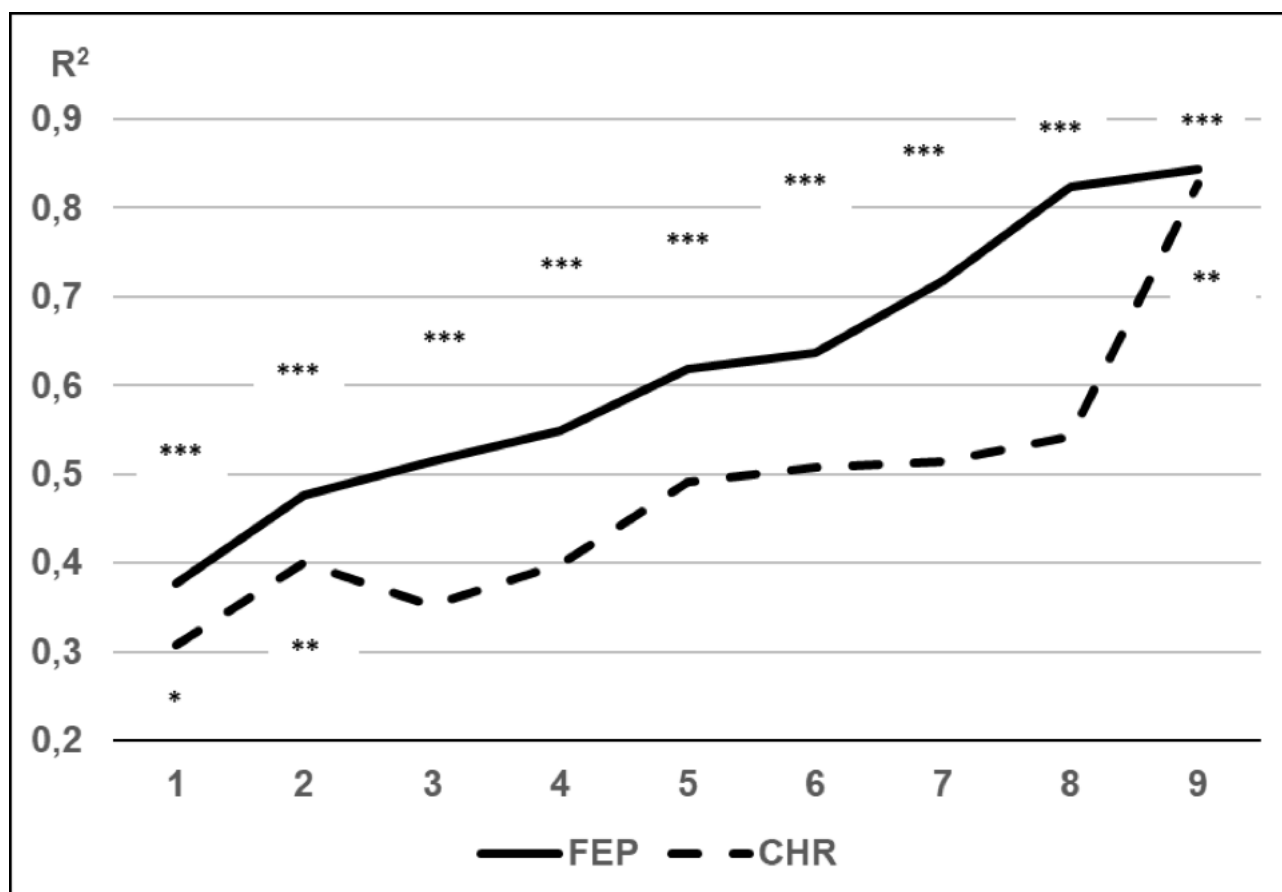
C. CHR

R² 0.149	B	p	CI95%	
Emotional poverty	-10.378	0.003	-17.075	-3.681

In the regression models for FEP patients, the proportion of explained variance (R²) increased steadily when explanatory factors were added, and the regression models were statistically significant at each stage. In CHR patients, the effects of PAS dimensions were significant. Thereafter, regression models were non-significant until the follow-up depression/anxiety dimension was included. Simultaneously, R² increased considerably (Figure 1).

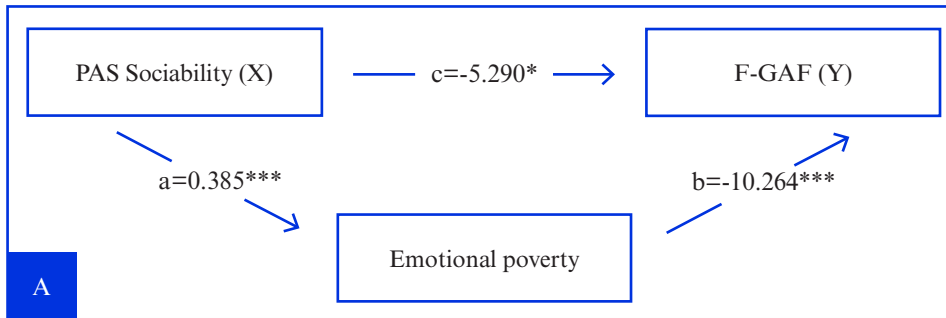
In mediation analyses of the total sample (Figure 2) and in FEP and CHR patients separately (Supplementary Figures 2a-2d), the effects of PAS Sociability and PAS Scholastic Performance on F-GAF were significantly mediated via SIPS Emotional Poverty. This finding explains why SIPS Emotional Poverty was not included into the regression model. In the total sample and FEP patients separately, the direct effect of PAS Sociability and Scholastic Performance on F-GAF was also significant, but not in CHR patients. Other SIPS dimensions and Childhood Trauma and NEUPSY dimensions and social support scores did not act as mediators between PAS and F-GAF.

Figure 1. Proportions of explained variation (R²) in prediction models by stages of added explanatory factors in linear regression analyses for the patients with first-episode psychosis (FEP) and clinical high risk for psychosis (CHR)



Predictors: 1. Premorbid (PAS) Scholastic performance; 2. previous and premorbid (PAS) Sociability; 3. previous and Trauma and Distress Scale (TADS) dimension; 4. previous and neuropsychological (NEUPSY) dimensions; 5. previous and social support (PSSS-R) scores; 6. previous and Structured Interview for Prodromal Syndromes (SIPS) dimensions; 7. previous and background factors; 8. previous and follow-up Psychoticism; 9. previous and follow-up Depression/Anxiety
Significance of regression models in each stage: *** p<0.001, ** p<0.01, * p<0.05

Figure 2. Path analyses for the effects of Premorbid Adjustment Scale (PAS) Sociability (A) and PAS Scholastic Performance (B) to follow-up functioning (F-GAF, Global Assessment of Functioning)



Note:

Total effect of X on Y

Effect	se	t	p	LLCI	ULCI
-9.240	2.467	-3.745	<0.001	-14.109	-4.370

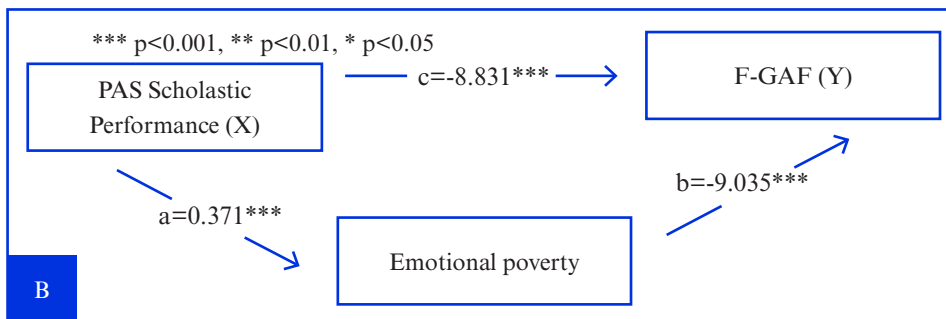
Direct effect of X on Y

Effect	se	t	p	LLCI	ULCI
-5.290	2.556	-2.070	0.040	-10.336	0.245

Indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
Emotional Poverty	-3.949	1.158	-6.409	-1.914

*** p<0.001, ** p<0.01, * p<0.05



Note:

Total effect of X on Y

Effect	se	t	p	LLCI	ULCI
-12.184	2.386	-5.107	<0.001	-16.892	-7.475

Direct effect of X on Y

Effect	se	t	p	LLCI	ULCI
-8.831	2.478	-3.564	<0.001	-13.722	-3.940

Indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
Emotional Poverty	-3.353	1.036	-5.497	-1.514

*** p<0.001, ** p<0.01, * p<0.05

Additionally, in the total sample and in FEP patients separately, the effect of PAS Sociability on F-GAF was significantly mediated via employment situation (all: effect -1.944; CI -3.709 to -0.516; FEP: effect -2.554; CI -4.799 to -0.724), but the effect of PAS School Performance on F-GAF was not mediated significantly via employment situation. In CHR individuals, the effect of PAS Sociability or Scholastic Performance on F-GAF was not mediated via work situation. In these analyses for all patients and FEP and CHR patients separately, employment situation was significantly associated ($p < 0.05$) with F-GAF.

DISCUSSION

DISORGANIZED THINKING AND DIMINISHED EMOTIONALITY: CORE FEATURES OF PSYCHOSES

In the combined sample of FEP and CHR patients, four dimensions, emotional distress, emotional poverty, disorganized thinking and delusions/hallucinations, were formed from the SIPS symptoms. Numerous previous factor analyses on patients with schizophrenia [81,82,83,84,85,86,87,88,89,90,91,92,93,94,95], on a heterogeneous group of psychiatric patients [96], early affective and non-affective psychoses [97] and on help-seeking youths with early FEP or CHR [98] have yielded negative, disorganized, affective and psychotic symptom dimensions resembling the symptom dimensions found in the present study. Names of dimensions may vary between different studies, but the SIPS symptom dimensions found in the present study fit quite well with the four main symptom dimensions found in other studies.

Of note, the SIPS items social anhedonia/withdrawal and avolition loaded on both emotional distress and emotional poverty dimensions, indicating that these symptom dimensions describing acute decreases in mood (depression) and long-standing decreases in emotional responsiveness (negative symptoms) are partly joined together [99]. Additionally, the SIPS item odd behaviour/appearance loaded on Emotional Poverty and Disorganized Thinking dimensions describing an inability to take care of cleanliness and appearance and inability to behave coherently having the same origin as Disorganized Thinking.

DISORGANIZED THINKING AND DIMINISHED EMOTIONALITY: MAJOR PREDICTORS OF FUNCTIONAL OUTCOMES

Kraepelin [1] and Bleuler [2], who both intensively followed their patients for years, regarded thought and emotional disturbances as essential features in psychotic disorders. The former spoke about the disturbed course of thoughts and emotional dullness, and the latter spoke about the loosening of associations and flattening of affect. The Disorganized Thinking and Emotional Poverty symptom dimensions come close to Kraepelin's and Bleuler's symptom descriptions and support Liddle's [100] suggestion that diminished mental activity (psychomotor poverty) and disorganization form core deficits of classic schizophrenia, even core features of schizotypal and CHR subjects.

In line with previous studies concerning negative symptoms and their central components [7,8,18,22,23,101,102] and formal thought disorders [103], emotional poverty and disorganized thinking, in the present study, were strongly correlated with poor functioning (F-GAF). In regression models, Emotional Poverty's effect on F-GAF was explained by PAS dimensions, except in the CHR sample. Thus, disorganized thinking and emotional poverty seem to have major independent effects on functional outcomes and probably different neural correlates, which are described in the Appendix.

Instead, in line with previous studies [104,105,106,107,108,109], the dimension including delusions and hallucinations and Bleulerian accessory symptoms played no role in the prediction of functional outcome. This finding concerns CHR patients specifically. The CHR cases are most often defined by subclinical delusional and hallucinatory symptoms, and their severity predicts conversion to psychosis [110]. However, more than 70% of CHR patients did not become psychotic during two years of follow-up [111]. Transition to psychosis hardly has much effect on functioning in the long run, and successful interventions preventing transition to psychosis have not improved the functional outcome of patients with CHR [112].

FUNCTIONAL OUTCOME HAS ITS ROOTS IN EARLY PREMORBID ADJUSTMENT

Premorbid adjustment is generally considered a global factor. In the present study, PAS was factorized into two separate dimensions: sociability and scholastic performance. Regression analyses showed that scholastic performance had a stronger association with functioning

than sociability, but sociability had an independent effect on functioning.

In line with previous studies, both premorbid dimensions correlated with emotional poverty and functional outcome [7,8,16,17,18,19,22,23,104,113,114] both directly and via emotional poverty so strongly that in regression modelling, emotional poverty did not enter the model in FEP patients. In the CHR patients, however, the effect of PAS dimensions was totally mediated via emotional poverty, whose association with functioning was emphasized as in another CHR study [115].

The fact that the effects of premorbid sociability and scholastic performance on F-GAF were mediated via emotional poverty but not via disorganized thinking, which had only a direct effect on F-GAF, indicates that emotional poverty has its roots in the very early psychosocial development of patients with psychosis. Contrary to a previous meta-analysis [36], in the present study, childhood adversity had no association with functional outcome.

CHR PATIENTS SUFFER FROM AFFECTIVE DISORDERS

While the baseline Delusion/Hallucination dimension and transition to psychosis [75] had no effect on F-GAF and the effect of follow-up Psychoticism on F-GAF was moderate, the follow-up Depression/Anxiety dimension increased strongly explanatory power in the regression model indicating that in CHR patients, continuation of affective symptomatology is more strongly associated with decreased functioning than psychotic symptoms. Moreover, the effect of both premorbid sociability and scholastic performance on F-GAF was mediated via emotional poverty. This, together with the finding concerning follow-up affective symptoms, indicates that there is an affective continuum from premorbid stage via baseline emotional poverty and follow-up depression/anxiety to deficits of functioning. In patients with depression, poor premorbid adjustment is associated with negative symptoms [99], indicating that negative symptoms are not specific to psychoses but are also found in depression. Moreover, in a study of CHR patients, lower levels of negative and mood/anxiety symptoms were related to an increased likelihood of both symptomatic and functional recovery [116].

The discussion above and the fact that disorganized thinking played no role in predicting functioning in CHR patients suggest that the CHR group fundamentally differs from the FEP group and, BLIPS excluded, represents a

group of affective disorders with temporary or durable psychotic-like symptoms indicating the severity of affective disorders. In a long-term outcome study of CHR patients, SIPS disorganized symptoms predicted functional outcomes [110]. However, SIPS disorganization symptoms represent a heterogeneous group that also includes negative symptoms (in the present factor analysis, 'odd behaviour and appearance' was partly loaded on Emotional Poverty, also representing negative symptoms).

For functional outcome, these findings challenge the CHR/Ultra-High Risk (UHR) paradigm. A great majority of CHR patients have non-psychotic clinical disorders, mostly anxiety and depression [117,118,119], as in the present study, and the occurrence of anxiety and depressive disorders is associated with impaired global functioning and suicidality [68,118]. Among UHR patients, affective symptoms, not subthreshold psychotic symptoms, are the most commonly reported reasons to seek help, and patients reporting affective symptoms had poorer functional outcomes than patients with subthreshold psychotic symptoms [119]. In a 6-year follow-up study, 45% of non-converted UHR patients remained functionally impaired, and persistence or recurrence of non-psychotic comorbid mental disorders was associated with poorer global functional outcomes [120]. All these findings strongly indicate that in the great majority of patients with CHR, the focus of attention should shift from prevention of transition to psychosis to active interventions of actual affective clinical disorders [121].

WORK STATUS IS A CENTRAL INDICATOR OF FUNCTIONAL OUTCOME IN FEP

Baseline work status was an independent, non-clinical predictor of functional outcome in patients with FEP. Contrary to FEP patients, in CHR patients, work status played no role in the prediction of functional outcome, emphasizing a basic difference between FEP and CHR patients. Although neurocognitive deficits are common in FEP [25,26,27,28,29,30,122] and in CHR patients [60,61,62,63,64,58] and, in the present study, correlated with GAFT0, they, in line with some other studies [31,110], did not predict functional outcome in our modelling in which premorbid school performance and emotional poverty, as in a network analysis [123], and work situation explained the effect of baseline neurocognitive deficits on functional outcome. Similarly, although social support correlated strongly with F-GAF, in modelling, its effect on functional outcome was explained away by premorbid sociability,

indicating that perceived social support at the time of onset of psychosis has its roots in premorbid social and peer relations. Baseline work status is a result of long-term development affected by several preceding and current factors, such as premorbid adjustment, neurocognitive performance, and deficit (emotional) and productive (positive) clinical symptoms, and is therefore one of the most important factors when treatment interventions are planned.

ADVANTAGES AND LIMITATIONS

Moderately low number of study participants limits results' generalizability. Also, the follow-up period (18 months) can be seen as a limitation. However, the first two years form the most important period in treatment of psychotic patients. Thereafter, the changes in patients' functioning are smaller (e.g., 171). The GAF, which measures mainly illness-related functioning, was used as an indicator of functioning. This finding may have emphasized associations between symptoms and GAF scores, especially at the baseline examination. In any case, GAF is a good enough indicator of real-life functioning. The small number of CHR subjects limits the generalizability of the CHR group findings. On the other hand, we were able to collect follow-up GAFs from all except two subjects, which clearly strengthens the certainty of the conclusions. We also believe that assessment of GAF scores from case notes and phone interviews gave a sufficiently reliable picture of the real-life functioning of the patients dropping out of treatment. A considerable number (18%) of TADS and social support questionnaires remained incomplete. However, GAF scores between the patients who did or did not complete the questionnaires (analyses available by request) did not differ significantly. In the present study, individual treatment interventions and their possible effects on functional outcome were not assessed. These aspects will be presented in later publications. Preliminarily, no association was found between baseline medication and follow-up functioning [75].

IMPLICATIONS

Regarding the functional outcomes of patients with psychosis, the significance of positive psychotic symptoms, although central in the diagnostic process, is minor. In the present study, the delusion/hallucination dimension played no role in predicting follow-up functioning because these symptoms remitted spontaneously or due to antipsychotic medication that was given to 90% of FEP patients.

Emotional poverty and disorganized thinking are the key clinical factors affecting functioning, and therefore, deserve major diagnostic weight in the group of functional psychotic disorders. Concerning emotional poverty, psychosocial interventions (e.g., cognitive behavioural therapy and cognitive remediation [124], social skills training), pharmacological medication (e.g., partial dopamine agonists, antidepressants and other pro-dopaminergic drugs) and non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation [125]) should start from the earliest stage of the illness.

Special rehabilitative measures for improving functioning can be directed towards studying and working [126]. We have a considerable amount of evidence that supporting education and employment can improve school participation and the ability to work in FEP patients [127], and that individual placement and support (IPT) can improve the ability to work and learn, leading to competitive employment when compared with traditional vocational rehabilitation [128]. Neurocognitive remediation combined with supported employment may further improve severely mentally ill patients' working ability [129,130].

In CHR patients, who most often suffer from affective disorders, the primary focus of interventions should be on the active treatment of these clinical disorders [131] and to consider the treatment of subclinical psychotic symptoms. There is some evidence that in CHR patients, mood disorders are associated with transition to psychosis [117]. Thus, it is possible that in addition to prevention of transition to psychosis, intensive interventions for mood disorders will improve the functioning of CHR patients more than interventions narrowly focused on prevention of the onset of psychosis. To further improve their functioning, the most severely ill CHR patients need the same psychosocial interventions as described above for psychotic patients. However, because lower momentary self-esteem seems to be associated with an increased intensity of psychotic experiences in daily life, self-esteem support interventions may reduce the intensity of, and distress caused by, psychotic experiences and prevent illness progression in both CHR and FEP patients at an early stage of their illness [132].

APPENDIX

*NEURAL CORRELATES OF DISORGANIZED THINKING AND EMOTIONAL POVERTY**1. Disorganized thinking – Deficit in neural coherence*

What is the possible neural basis of disorganized thinking? Both Kraepelin [37] and Bleuler [2] proposed that psychosis was a disease of the cortex. Neuroimaging research has verified that psychotic patients have extensive defects in their cortex (grey matter) and subcortical structures (white matter) [133,134]. Deficits of white matter, indicating altered myelination, are also associated with lower regional grey matter volumes (synaptic layer) and poor outcomes in schizophrenia [135].

Weinberger et al. [136] hypothesized that schizophrenia is a disorder of neuronal connectivity. This dysconnectivity may be due to alterations in neural myelination [135] and/or synaptic pruning [137] reaching its peak at puberty when disorganized symptomatology manifests in psychotic states. Deficits in myelination may lead to lengthening and scattering conduction times (dysconnectivity) and reduced capacity of the neural system to synchronize particular neural frequencies (desynchronization) [138], while excessive pruning may result in diminished, blocked, or otherwise disturbed connectivity (dysconnectivity), and the occurrence of delusions and hallucinations may be possible [139]. These deficits in myelination and neuropil connections affect various neural tracts and cortex areas and can manifest as various forms of disorganization in thinking, speaking, perception and behaviour. Formal thought disorders in schizophrenia are often, but not always, associated with structural and functional aberrations in the language network (e.g., the inferior frontal gyrus; Brodmann Area, the frontal operculum, the superior temporal gyrus, the middle temporal gyrus) [140], suggesting that thought disorders are indicators of extensive neural dysconnectivity.

Disorganized thinking may relate to disturbed neural conduction and connections with difficulties in synchronizing and coherently directing stimuli from multimodal sources [141]. One candidate of these sources is the cerebellum [142] and the cerebello-thalamo-cortical circuitry [143]. Increased connectivity in the cerebello-thalamo-cortical circuitry is a pattern found in patients with CHR (more pronounced in converters) and schizophrenia associated with disorganized symptoms [144]. Increased connectivity in the cerebello-thalamo-cortical circuitry may be a heritable trait associated with the genetic risk of schizophrenia [145].

Signs of thought disorders are often seen in close relatives of patients with schizophrenia [146,147], further suggesting that disorganized thinking and its neural correlates may have a genetic background.

Disorganized thinking and behaviour manifest most clearly at the acute phase of psychosis. In acute psychosis, vigorous turmoil of synaptic transmitters due to overactivity of basal structures [148,149] and axonal leakage of electric signals violate connectivity of the genetically vulnerable neural network, and consequently lead to incoherent (synaptic level) and idiosyncratic (signal leaking) thinking and behaviour. During recovery from psychosis, disorganized thinking decreases [150] but retains its significance as an indicator of poor outcome, even if it is hardly detectable anymore. However, even in a recovered stage, there are signs of neural disorganization, such as impaired facial emotion recognition [151] and emotion-specific (neural) face processing [152]. In the case of schizophrenia, “restitutio ad integrum” does not occur [2]. Repetitive psychotic episodes may have toxic effects on the unstable neural network and lead to chronic thought disorders. Neuroleptics, such as synaptic blockers and anti-inflammatory [153] agents, can facilitate the recovery of acute processes but have little effect on long-term functional outcomes. In follow-up studies, daily doses of neuroleptics mainly correlate with the severity of illness.

In summary, in patients with psychosis, disorganized thinking seems to be an indicator of a general structural and functional disorganization of the central nervous system, and the magnitude of its effect on functional outcome depends on the extent of neural disorganization.

2. Emotional Poverty – Deficit in neural energizing processes

Contrary to disorganized thinking, which manifests after puberty, emotional poverty has its roots in early childhood/adolescence. Premorbid sociability and scholastic performance comprise emotional and cognitive components of apathy that are typical in schizophrenia [154] but are also found in depression [99] and across different pathological conditions [155]. Very recently, in an 18-month follow-up study, the negative factor characterized by high negative symptoms and high premorbid deficits was loaded over patient groups with ROP (Recent Onset of Psychosis) (55%), CHR (31%) and non-psychotic depression (14%) [156]. Additionally, in the present study, sociability correlated with the distress dimension, indicating its association with depression/anxiety symptomatology. Thus, emotional poverty is not specific to psychotic disorders but also relates

to other disorders, particularly to depression. Regarding depression, the distinction between primary (“thought to be intrinsic to the pathophysiology of schizophrenia”) and secondary (“thought to be related to other factors, such as psychiatric or medical comorbidities, treatment adverse effects or environmental factors”) negative symptoms may be artificial [156].

Neuroimaging studies have suggested that abnormalities within the fronto-basal ganglia network, including the thalamus [155,156,157,158,159], structures representing motivation-relation circuits [160,161], are most consistently associated with apathy, a key component of negative symptoms, across the different pathological conditions. Emotional apathy is associated with damage to the orbitofrontal (ventromedial prefrontal) cortex ventral striatum and the anterior cingulate cortex, while cognitive apathy correlates with the dorsolateral prefrontal cortex and dorsal caudate nuclei [158,162]. Kirschner et al. [163] suggested that orbitofrontal-striatal abnormalities associated with negative symptoms may predate the occurrence of schizophrenia.

Recently, Wang et al. [164] found that the intrinsic functional connectivity and structural properties (fractional anisotropy and fibers) of the left frontal white matter corresponded to individual negative symptoms in adolescent-onset schizophrenia. A decreased number of fibers in the serotonergic network (raphe nuclei, anterior and posterior cingulate cortices, and prefrontal and inferior parietal cortices) and frontal white matter cingulum network contributed to negative symptom severity. There was also abnormal functional and structural connectivity between the interhemispheric frontal white matter; the decreased fiber counts between frontal hemispheres correlated inversely with the negative symptoms. The finding regarding the serotonergic neural network is interesting. Serotonergic antidepressants have some effect on negative symptoms in patients with schizophrenia [165]. More specifically, the 5-HT_{2A} receptor has been considered a potential target for reducing negative and cognitive deficits [166]. Mirtazapine, an antidepressant with 5HT_{2A} antagonistic properties [167], has been effective in reducing negative symptoms in patients with schizophrenia [168], and roluperidone, an antipsychotic agent with a 5HT_{2A} receptor antagonist, has improved reduced emotional experience (avolition-anhedonia) and reduced emotional expression (affective blunting and alogia), which are key components of negative symptoms [169]. Another study related to roluperidone also emphasized the central role of avolition within the treatment of negative symptoms

[170]. However, the role of the serotonergic network in negative symptoms is unclear.

In summary, emotional poverty seems not to be specific to psychosis but reflects unspecific deficits in neural structures related to motivational and energizing Central Nervous System processes, and can manifest as difficulties in psychosocial relations and intellectual performance in childhood and adolescence.

Supplementary Material

Supplementary data are available at [Psychiatria Fennica online](https://www.psychiatria.fennica.fi/).

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Declaration of interest

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References

1. Kraepelin E. Psychiatrie - Ein Lehrbuch für Studierende und Ärzte. Sechste, vollständig umgearbeitete Auflage. Verlag von Johan Ambrosius Barth, Leipzig, 1899.
2. Bleuler E. Dementia Praecox oder die Gruppe der Schizophrenien. Translation Dementia Praecox or the group of schizophrenias. International University Press, New York 1911/1950.
3. Schneider K. Clinical psychopathology. Grune and Stratton, New York, 1959.
4. Hawk AB, Carpenter WT Jr, Strauss JS. Diagnostic criteria and five-year outcome in schizophrenia. A report from the International Pilot Study of schizophrenia. Arch Gen Psychiatry. 1975 Mar;32(3):343-7. doi: 10.1001/archpsyc.1975.01760210077005. PMID: 1115575.
5. Langfeldt G. The schizophreniform states. Munksgaard, Köbenhavn 1939.
6. Garmezy N, Rodnic EH. Premorbid adjustment and performance in schizophrenia: implications for interpreting heterogeneity in schizophrenia. J Nerv Ment Dis. 1959 Nov;129:450-66. doi: 10.1097/00005053-195911000-00006. PMID: 13826597.
7. Salokangas RKR. Skitsofreniaan sairastuneiden psykososiaalinen kehitys. (English Summary: The psychosocial development of schizophrenic patients.) Kansaneläkelaitoksen julkaisuja AL 7, Turku,1977.
8. Salokangas RKR. Skitsofrenian hoito ja ennuste. (English Summary: Treatment and outcome in schizophrenia.) Kansanterveystieteen julkaisuja M 89/85. Tampereen yliopiston kansanterveystieteen laitos ja Turun yliopiston Psykiatrian klinikka, Tampere 1985.
9. Strauss JS, Carpenter WT Jr, Bartko JJ. The diagnosis and understanding of schizophrenia. Summary and conclusions. Schizophr Bull. 1974 Winter;(11):70-80. PMID: 4619922.
10. Andreasen NC, Olsen S. Negative v positive schizophrenia. Definition and validation. Arch Gen Psychiatry. 1982 Jul;39(7):789-94. doi: 10.1001/archpsyc.1982.04290070025006. PMID: 7165478.
11. Vaillant GE. Prospective prediction of schizophrenic remission. Arch Gen Psychiatry. 1964 Nov;11:509-18. doi: 10.1001/archpsyc.1964.01720290051007. PMID: 14208654.
12. Astrup C, Noreik K. Functional psychoses. Diagnostic and prognostic models. Charles C Thomas. Springfield, 1966.

13. Noreik K, Astrup C, Dalgard OS, Holmboe R. A prolonged follow-up of acute schizophrenic and schizophreniform psychoses. *Acta Psychiatr Scand.* 1967;43(4):432-43. doi: 10.1111/j.1600-0447.1967.tb05780.x. PMID: 5582394.
14. Stephens JH, Astrup C, Mangrum JC. Prognosis in schizophrenia. Prognostic scales crossvalidated in American and Norwegian patients. *Arch Gen Psychiatry.* 1967 Jun;16(6):693-8. doi: 10.1001/archpsyc.1967.01730240049008. PMID: 6027367.
15. Stephens JH. Long-term prognosis and followup in schizophrenia. *Schizophr Bull.* 1978;4(1):25-47. doi: 10.1093/schbul/4.1.25. PMID: 34208.
16. Salokangas RKR. Psychosocial prognosis in schizophrenia. Formation of the prognosis for schizophrenic patients: a multivariate analysis. *Annales Universitatis Turkuensis. Ser. D. University of Turku, Turku* 1978.
17. Salokangas RK. Prognostic implications of the sex of schizophrenic patients. *Br J Psychiatry.* 1983 Feb;142:145-51. doi: 10.1192/bjp.142.2.145. PMID: 6839067.
18. Salokangas RK, Stengård E. Gender and short-term outcome in schizophrenia. *Schizophr Res.* 1990 Oct-Dec;3(5-6):333-45. doi: 10.1016/0920-9964(90)90019-4. PMID: 2282339.
19. Salokangas RKR, Stengård E, Rääköläinen V, Alanen YO, Kaljonen A. Uusien skitsofreniapotilaiden hoito ja ennuste (USP-projekti) V: Viiden vuoden ennuste. (Treatment of New Patients with Schizophrenia (NPS-project) V: Five-year follow-up). *Reports of Psychiatria Fennica No 95, Helsinki* 1991.
20. Salokangas RK, Honkonen T, Stengård E, Koivisto AM. To be or not to be married--that is the question of quality of life in men with schizophrenia. *Soc Psychiatry Psychiatr Epidemiol.* 2001 Aug;36(8):381-90. doi: 10.1007/s001270170028. PMID: 11766968.
21. Honkonen T, Stengård E, Virtanen M, Salokangas RK. Employment predictors for discharged schizophrenia patients. *Soc Psychiatry Psychiatr Epidemiol.* 2007 May;42(5):372-80. doi: 10.1007/s00127-007-0180-5. Epub 2007 Mar 19. PMID: 17492406.
22. Möller HJ, von Zerssen D. Course and outcome. In Hirsch SR, Weinberger DR eds. *Schizophrenia.* Blackwell Science, pp.106-127, Oxford 1995.
23. White C, Stirling J, Hopkins R, Morris J, Montague L, Tantam D, Lewis S. Predictors of 10-year outcome of first-episode psychosis. *Psychol Med.* 2009 Sep;39(9):1447-56. doi: 10.1017/S003329170800514X. Epub 2009 Feb 3. PMID: 19187566.
24. Tempelaar WM, Termorshuizen F, MacCabe JH, Boks MP, Kahn RS. Educational achievement in psychiatric patients and their siblings: a register-based study in 30 000 individuals in The Netherlands. *Psychol Med.* 2017 Mar;47(4):776-784. doi: 10.1017/S0033291716002877. Epub 2016 Nov 22. PMID: 27873559.
25. Pantelis C, Yücel M, Wood SJ, McGorry PD, Velakoulis D. Early and late neurodevelopmental disturbances in schizophrenia and their functional consequences. *Aust N Z J Psychiatry.* 2003 Aug;37(4):399-406. doi: 10.1046/j.1440-1614.2003.01193.x. PMID: 12873323.
26. Carpenter WT, Bustillo JR, Thaker GK, van Os J, Krueger RF, Green MJ. The psychoses: cluster 3 of the proposed meta-structure for DSM-V and ICD-11. *Psychol Med.* 2009 Dec;39(12):2025-42. doi: 10.1017/S0033291709990286. Epub 2009 Oct 1. PMID: 19796428.

27. Rosell DR, Futterman SE, McMaster A, Siever LJ. Schizotypal personality disorder: a current review. *Curr Psychiatry Rep.* 2014 Jul;16(7):452. doi: 10.1007/s11920-014-0452-1. PMID: 24828284; PMCID: PMC4182925.
28. Bortolato B, Miskowiak KW, Köhler CA, Vieta E, Carvalho AF. Cognitive dysfunction in bipolar disorder and schizophrenia: a systematic review of meta-analyses. *Neuropsychiatr Dis Treat.* 2015 Dec 17;11:3111-25. doi: 10.2147/NDT.S76700. PMID: 26719696; PMCID: PMC4689290.
29. Bora E, Pantelis C. Social cognition in schizophrenia in comparison to bipolar disorder: A meta-analysis. *Schizophr Res.* 2016 Aug;175(1-3):72-78. doi: 10.1016/j.schres.2016.04.018. Epub 2016 Apr 23. PMID: 27117677.
30. Green MF, Horan WP, Lee J. Nonsocial and social cognition in schizophrenia: current evidence and future directions. *World Psychiatry.* 2019 Jun;18(2):146-161. doi: 10.1002/wps.20624. PMID: 31059632; PMCID: PMC6502429.
31. Stirling J, White C, Lewis S, Hopkins R, Tantam D, Huddy A, Montague L. Neurocognitive function and outcome in first-episode schizophrenia: a 10-year follow-up of an epidemiological cohort. *Schizophr Res.* 2003 Dec 15;65(2-3):75-86. doi: 10.1016/s0920-9964(03)00014-8. PMID: 14630300.
32. Varese F, Smeets F, Drukker M, Lieverse R, Lataster T, Viechtbauer W, Read J, van Os J, Bentall RP. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophr Bull.* 2012 Jun;38(4):661-71. doi: 10.1093/schbul/sbs050. Epub 2012 Mar 29. PMID: 22461484; PMCID: PMC3406538.
33. Bonoldi I, Simeone E, Rocchetti M, Codjoe L, Rossi G, Gambi F, Balottin U, Caverzasi E, Politi P, Fusar-Poli P. Prevalence of self-reported childhood abuse in psychosis: a meta-analysis of retrospective studies. *Psychiatry Res.* 2013 Nov 30;210(1):8-15. doi: 10.1016/j.psychres.2013.05.003. Epub 2013 Jun 20. PMID: 23790604.
34. Trauelsen AM, Bendall S, Jansen JE, Nielsen HG, Pedersen MB, Trier CH, Haahr UH, Simonsen E. Childhood adversity specificity and dose-response effect in non-affective first-episode psychosis. *Schizophr Res.* 2015 Jun;165(1):52-9. doi: 10.1016/j.schres.2015.03.014. Epub 2015 Apr 11. PMID: 25868932.
35. Trotta A, Murray RM, Fisher HL. The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. *Psychol Med.* 2015;45(12):2481-98. doi: 10.1017/S0033291715000574. Epub 2015 Apr 23. PMID: 25903153.
36. Thomas S, Höfler M, Schäfer I, Trautmann S. Childhood maltreatment and treatment outcome in psychotic disorders: a systematic review and meta-analysis. *Acta Psychiatr Scand.* 2019 Oct;140(4):295-312. doi: 10.1111/acps.13077. Epub 2019 Sep 4. PMID: 31357235.
37. Kraepelin E. *Psychiatrie. Ein kurzes Lehrbuch für Studierende und Aerzte.* Zweite, gänzlich umgearbeitete Auflage. Leipzig: Verlag von Ambrosius Abel, Leipzig 1887.
38. Klosterkötter J, Schultze-Lutter F, Ruhrmann S. Kraepelin and psychotic prodromal conditions. *Eur Arch Psychiatry Clin Neurosci.* 2008 Jun;258 Suppl 2:74-84. doi: 10.1007/s00406-008-2010-5. PMID: 18516519.
39. Hoch P, Polatin P. Pseudoneurotic forms of schizophrenia. *Psychiatr Q.* 1949 Apr;23(2):248-76. doi: 10.1007/BF01563119. PMID: 18137714.
40. Hoch PH, Cattel JP, Strahl MO, Pennes HH. The course and outcome of pseudoneurotic schizophrenia. *Am J Psychiatry.* 1962 Aug;119:106-15. doi: 10.1176/ajp.119.2.106. PMID: 13907898.
41. Huber G. Reine Defektsyndrome und Basisstadien endogener Psychosen. *Fortschr. Neurol. Psychiatry.* 1966;34, 409-426.

42. Huber G, Gross G, Schüttler R, Linz M. Longitudinal studies of schizophrenic patients. *Schizophr Bull.* 1980;6(4):592-605. doi: 10.1093/schbul/6.4.592. PMID: 7444391.
43. Gross G, Huber G. Prodromes and primary prevention of schizophrenic psychoses. *Neurol. Psychiatry Brain Res.* 1998;6, 51-58.
44. Gross G, Huber G, Klosterkötter J, Linz M. BSABS Bonner Skala für die Beurteilung von Basissymptomen (Bonn Scale for the Assessment of Basic Symptoms). Manual, Kommentar, Dokumentationbogen. Springer, Berlin 1987.
45. Schultze-Lutter F, Addington J, Ruhrmann S, Klosterkötter J. Schizophrenia Proneness Instrument, Adult Version (SPI-A), 2007.
46. Yung AR, McGorry PD. The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophr Bull.* 1996;22(2):353-70. doi: 10.1093/schbul/22.2.353. PMID: 8782291.
47. Yung AR, Phillips LJ, McGorry PD, McFarlane CA, Francey S, Harrigan S, Patton GC, Jackson HJ. Prediction of psychosis. A step towards indicated prevention of schizophrenia. *Br J Psychiatry Suppl.* 1998;172(33):14-20. PMID: 9764121.
48. Yung AR, Jackson HJ. The onset of psychotic disorder: Clinical and research aspects. In: McGorry PD, Jackson HJ eds. *The recognition and management of early psychosis. A preventive approach.* Cambridge University Press, p. 27–50, Cambridge 1999.
49. McGlashan TH, Miller TJ, Woods SW. Structured interview for prodromal syndromes. Version 3.0. Yale School of Medicine, PRIME Research Clinic, Connecticut, New Haven 2001.
50. Miller TJ, McGlashan TH, Rosen JL, Somjee L, Markovich PJ, Stein K, Woods SW. Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. *Am J Psychiatry.* 2002 May;159(5):863-5. doi: 10.1176/appi.ajp.159.5.863. PMID: 11986145.
51. Fusar-Poli P, Salazar de Pablo G, Correll CU, Meyer-Lindenberg A, Millan MJ, Borgwardt S, Galderisi S, Bechdolf A, Pfennig A, Kessing LV, van Amelsvoort T, Nieman DH, Domschke K, Krebs MO, Koutsouleris N, McGuire P, Do KQ, Arango C. Prevention of Psychosis: Advances in Detection, Prognosis, and Intervention. *JAMA Psychiatry.* 2020 Jul 1;77(7):755-765. doi: 10.1001/jamapsychiatry.2019.4779. PMID: 32159746.
52. Yung AR, Phillips LJ, Yuen HP, Francey SM, McFarlane CA, Hallgren M, McGorry PD. Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophr Res.* 2003 Mar 1;60(1):21-32. doi: 10.1016/s0920-9964(02)00167-6. PMID: 12505135.
53. Cannon TD, Cadenhead K, Cornblatt B, Woods SW, Addington J, Walker E, Seidman LJ, Perkins D, Tsuang M, McGlashan T, Heinssen R. Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. *Arch Gen Psychiatry.* 2008 Jan;65(1):28-37. doi: 10.1001/archgenpsychiatry.2007.3. PMID: 18180426; PMCID: PMC3065347.
54. Ruhrmann S, Schultze-Lutter F, Salokangas RK, Heinimaa M, Linszen D, Dingemans P, Birchwood M, Patterson P, Juckel G, Heinz A, Morrison A, Lewis S, von Reventlow HG, Klosterkötter J. Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. *Arch Gen Psychiatry.* 2010 Mar;67(3):241-51. doi: 10.1001/archgenpsychiatry.2009.206. PMID: 20194824.

55. Fusar-Poli P, Bonoldi I, Yung AR, Borgwardt S, Kempton MJ, Valmaggia L, Barale F, Caverzasi E, McGuire P. Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Arch Gen Psychiatry*. 2012 Mar;69(3):220-9. doi: 10.1001/archgenpsychiatry.2011.1472. PMID: 22393215.
56. Fusar-Poli P, Cappucciati M, Borgwardt S, Woods SW, Addington J, Nelson B, Nieman DH, Stahl DR, Rutigliano G, Riecher-Rössler A, Simon AE, Mizuno M, Lee TY, Kwon JS, Lam MM, Perez J, Keri S, Amminger P, Metzler S, Kawohl W, Rössler W, Lee J, Labad J, Ziermans T, An SK, Liu CC, Woodberry KA, Braham A, Corcoran C, McGorry P, Yung AR, McGuire PK. Heterogeneity of Psychosis Risk Within Individuals at Clinical High Risk: A Meta-analytical Stratification. *JAMA Psychiatry*. 2016 Feb;73(2):113-20. doi: 10.1001/jamapsychiatry.2015.2324. PMID: 26719911.
57. Salokangas RK, Dingemans P, Heinimaa M, Svirskis T, Luutonen S, Hietala J, Ruhrmann S, Juckel G, Graf von Reventlow H, Linszen D, Birchwood M, Patterson P, Schultze-Lutter F, Klosterkötter J; EPOS group. Prediction of psychosis in clinical high-risk patients by the Schizotypal Personality Questionnaire. Results of the EPOS project. *Eur Psychiatry*. 2013 Oct;28(8):469-75. doi: 10.1016/j.eurpsy.2013.01.001. Epub 2013 Feb 8. PMID: 23394823.
58. Bolt LK, Amminger GP, Farhall J, McGorry PD, Nelson B, Markulev C, Yuen HP, Schäfer MR, Mossaheb N, Schlögelhofer M, Smesny S, Hickie IB, Berger GE, Chen EYH, de Haan L, Nieman DH, Nordentoft M, Riecher-Rössler A, Verma S, Thompson A, Yung AR, Allott KA. Neurocognition as a predictor of transition to psychotic disorder and functional outcomes in ultra-high risk participants: Findings from the NEURAPRO randomized clinical trial. *Schizophr Res*. 2019 Apr;206:67-74. doi: 10.1016/j.schres.2018.12.013. Epub 2018 Dec 14. PMID: 30558978.
59. Cotter J, Drake RJ, Bucci S, Firth J, Edge D, Yung AR. What drives poor functioning in the at-risk mental state? A systematic review. *Schizophr Res*. 2014 Nov;159(2-3):267-77. doi: 10.1016/j.schres.2014.09.012. Epub 2014 Sep 24. PMID: 25261041.
60. Niendam TA, Bearden CE, Johnson JK, McKinley M, Loewy R, O'Brien M, Nuechterlein KH, Green MF, Cannon TD. Neurocognitive performance and functional disability in the psychosis prodrome. *Schizophr Res*. 2006 May;84(1):100-11. doi: 10.1016/j.schres.2006.02.005. Epub 2006 Mar 24. PMID: 16563699.
61. Eslami A, Jahshan C, Cadenhead KS. Disorganized symptoms and executive functioning predict impaired social functioning in subjects at risk for psychosis. *J Neuropsychiatry Clin Neurosci*. 2011 Fall;23(4):457-60. doi: 10.1176/jnp.23.4.jnp457. PMID: 22231319; PMCID: PMC4113423.
62. Lin A, Wood SJ, Nelson B, Brewer WJ, Spiliotacopoulos D, Bruxner A, Broussard C, Pantelis C, Yung AR. Neurocognitive predictors of functional outcome two to 13 years after identification as ultra-high risk for psychosis. *Schizophr Res*. 2011 Oct;132(1):1-7. doi: 10.1016/j.schres.2011.06.014. Epub 2011 Jul 16. PMID: 21763109.
63. Carrión RE, McLaughlin D, Goldberg TE, Auther AM, Olsen RH, Olvet DM, Correll CU, Cornblatt BA. Prediction of functional outcome in individuals at clinical high risk for psychosis. *JAMA Psychiatry*. 2013 Nov;70(11):1133-42. doi: 10.1001/jamapsychiatry.2013.1909. PMID: 24006090; PMCID: PMC4469070.
64. Glenthøj LB, Fagerlund B, Hjorthøj C, Jepsen JRM, Bak N, Kristensen TD, Wenneberg C, Krakauer K, Roberts DL, Nordentoft M. Social cognition in patients at ultra-high risk for psychosis: What is the relation to social skills and functioning? *Schizophr Res Cogn*. 2016 Jul 8;5:21-27. doi: 10.1016/j.scog.2016.06.004. PMID: 28740813; PMCID: PMC5514303.
65. Addington J, Stowkowy J, Cadenhead KS, Cornblatt BA, McGlashan TH, Perkins DO, Seidman LJ, Tsuang MT, Walker EF, Woods SW, Cannon TD. Early traumatic experiences in those at clinical high risk for psychosis. *Early Interv Psychiatry*. 2013 Aug;7(3):300-5. doi: 10.1111/eip.12020. Epub 2013 Jan 24. PMID: 23343384; PMCID: PMC3754436.

66. Kraan TC, Ising HK, Fokkema M, Velthorst E, van den Berg DPG, Kerkhoven M, Veling W, Smit F, Linszen DH, Nieman DH, Wunderink L, Boonstra N, Klaassen RMC, Dragt S, Rietdijk J, de Haan L, van der Gaag M. The effect of childhood adversity on 4-year outcome in individuals at ultra high risk for psychosis in the Dutch Early Detection Intervention Evaluation (EDIE-NL) Trial. *Psychiatry Res.* 2017 Jan;247:55-62. doi: 10.1016/j.psychres.2016.11.014. Epub 2016 Nov 11. PMID: 27863320.
67. Kraan T, van Dam DS, Velthorst E, de Ruigh EL, Nieman DH, Durston S, Schothorst P, van der Gaag M, de Haan L. Childhood trauma and clinical outcome in patients at ultra-high risk of transition to psychosis. *Schizophr Res.* 2015 Dec;169(1-3):193-198. doi: 10.1016/j.schres.2015.10.030. Epub 2015 Nov 14. PMID: 26585219.
68. Salokangas RKR, Patterson P, Hietala J, Heinimaa M, From T, Ilonen T, von Reventlow HG, Schultze-Lutter F, Juckel G, Linszen D, Dingemans P, Birchwood M, Klosterkötter J, Ruhrmann S; EPOS group. Childhood adversity predicts persistence of suicidal thoughts differently in females and males at clinical high-risk patients of psychosis. Results of the EPOS project. *Early Interv Psychiatry.* 2019 Aug;13(4):935-942. doi: 10.1111/eip.12714. Epub 2018 Jul 23. PMID: 30033690.
69. Addington J, Penn D, Woods SW, Addington D, Perkins DO. Social functioning in individuals at clinical high risk for psychosis. *Schizophr Res.* 2008 Feb;99(1-3):119-24. doi: 10.1016/j.schres.2007.10.001. Epub 2007 Nov 19. PMID: 18023329; PMCID: PMC2292799.
70. Salokangas RK, Heinimaa M, From T, Löyttyniemi E, Ilonen T, Luutonen S, Hietala J, Svirskis T, von Reventlow HG, Juckel G, Linszen D, Dingemans P, Birchwood M, Patterson P, Schultze-Lutter F, Ruhrmann S, Klosterkötter J; EPOS group. Short-term functional outcome and premorbid adjustment in clinical high-risk patients. Results of the EPOS project. *Eur Psychiatry.* 2014 Aug;29(6):371-80. doi: 10.1016/j.eurpsy.2013.10.003. Epub 2013 Dec 7. PMID: 24315804.
71. Koutsouleris N, Kambeitz-Ilankovic L, Ruhrmann S, Rosen M, Rued A, Dwyer DB, Paolini M, Chisholm K, Kambeitz J, Haidl T, Schmidt A, Gillam J, Schultze-Lutter F, Falkai P, Reiser M, Riecher-Rössler A, Upthegrove R, Hietala J, Salokangas RKR, Pantelis C, Meisenzahl E, Wood SJ, Beque D, Brambilla P, Borgwardt S; PRONIA Consortium. Prediction Models of Functional Outcomes for Individuals in the Clinical High-Risk State for Psychosis or With Recent-Onset Depression: A Multimodal, Multisite Machine Learning Analysis. *JAMA Psychiatry.* 2018 Nov 1;75(11):1156-1172. doi: 10.1001/jamapsychiatry.2018.2165. Erratum in: *JAMA Psychiatry.* 2019 May 1;76(5):550. PMID: 30267047; PMCID: PMC6248111.
72. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. *Schizophr Bull.* 1982;8(3):470-84. doi: 10.1093/schbul/8.3.470. PMID: 7134891.
73. McGlashan T, Walsh B, Woods S. *The psychosis-risk syndrome: handbook for diagnosis and follow-up.* Oxford University Press, USA 2010.
74. Salokangas RKR, From T, Ilonen T, Luutonen S, Heinimaa M, Armio RL, Laurikainen H, Walta M, Paju J, Toivonen A, Jalo P, Tuominen L, Hietala J. Short-term functional outcome in psychotic patients: results of the Turku early psychosis study (TEPS). medRxiv. doi: <https://doi.org/10.1101/2021.02.05.21251198>.
75. Salokangas RKR, From T, Ilonen T, Luutonen S, Heinimaa M, Armio RL, Laurikainen H, Walta M, Paju J, Toivonen A, Jalo P, Tuominen L, Hietala J. Short-term functional outcome in psychotic patients: results of the Turku early psychosis study (TEPS). *BMC Psychiatry.* 2021 Dec 2;21(1):602. doi: 10.1186/s12888-021-03516-4. PMID: 34856968; PMCID: PMC8641211.
76. First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P)* Biometrics Research, New York State Psychiatric Institute, New York 2002.
77. Patterson P, Skeate A, Schultze-Lutter F, Graf von Reventlow H, Wieneke A, Ruhrmann S, Salokangas R. *The Trauma and Distress Scale.* University of Birmingham, Birmingham, UK 2002.

78. Salokangas RK, Schultze-Lutter F, Patterson P, von Reventlow HG, Heinimaa M, From T, Luutonen S, Hankala J, Kotimäki M, Tuominen L. Psychometric properties of the Trauma and Distress Scale, TADS, in an adult community sample in Finland. *Eur J Psychotraumatol*. 2016 Mar 30;7:30062. doi: 10.3402/ejpt.v7.30062. PMID: 27032511; PMCID: PMC4816812.
79. Blumenthal JA, Burg MM, Barefoot J, Williams RB, Haney T, Zimet G. Social support, type A behavior, and coronary artery disease. *Psychosom Med*. 1987 Jul-Aug;49(4):331-40. doi: 10.1097/00006842-198707000-00002. PMID: 3615762.
80. Hayes AF. PROCESS procedure for SPSS release 2.13.2. 2014. [Computer software]. Retrieved from. <http://www.processmacro.org>. (Accessed 10 January 2023) 2014.
81. Bilder RM, Mukherjee S, Rieder RO, Pandurangi AK. Symptomatic and neuropsychological components of defect states. *Schizophr Bull*. 1985;11(3):409-19. doi: 10.1093/schbul/11.3.409. PMID: 4035304.
82. Liddle PF. The symptoms of chronic schizophrenia. A re-examination of the positive-negative dichotomy. *Br J Psychiatry*. 1987 Aug;151:145-51. doi: 10.1192/bjp.151.2.145. PMID: 3690102.
83. Kay SR, Sevy S. Pyramidal model of schizophrenia. *Schizophr Bull*. 1990;16(3):537-45. doi: 10.1093/schbul/16.3.537. PMID: 2287938.
84. Arndt S, Andreasen NC, Flaum M, Miller D, Nopoulos P. A longitudinal study of symptom dimensions in schizophrenia. Prediction and patterns of change. *Arch Gen Psychiatry*. 1995 May;52(5):352-60. doi: 10.1001/archpsyc.1995.03950170026004. PMID: 7726715.
85. Keefe RS, Harvey PD, Lenzenweger MF, Davidson M, Apter SH, Schmeidler J, Mohs RC, Davis KL. Empirical assessment of the factorial structure of clinical symptoms in schizophrenia: negative symptoms. *Psychiatry Res*. 1992 Nov;44(2):153-65. doi: 10.1016/0165-1781(92)90049-9. PMID: 1480680.
86. Peralta V, de Leon J, Cuesta MJ. Are there more than two syndromes in schizophrenia? A critique of the positive-negative dichotomy. *Br J Psychiatry*. 1992 Sep;161:335-43. doi: 10.1192/bjp.161.3.335. PMID: 1356572.
87. von Knorring L, Lindström E. Principal components and further possibilities with the PANSS. *Acta Psychiatr Scand Suppl*. 1995;388:5-10. doi: 10.1111/j.1600-0447.1995.tb05937.x. PMID: 7541600.
88. Lindenmayer JP, Bernstein-Hyman R, Grochowski S. Five-factor model of schizophrenia. Initial validation. *J Nerv Ment Dis*. 1994 Nov;182(11):631-8. doi: 10.1097/00005053-199411000-00006. PMID: 7964671.
89. Andreasen NC, Arndt S, Alliger R, Miller D, Flaum M. Symptoms of schizophrenia. Methods, meanings, and mechanisms. *Arch Gen Psychiatry*. 1995 May;52(5):341-51. doi: 10.1001/archpsyc.1995.03950170015003. PMID: 7726714.
90. Arndt S, Alliger RJ, Andreasen NC. The distinction of positive and negative symptoms. The failure of a two-dimensional model. *Br J Psychiatry*. 1991 Mar;158:317-22. doi: 10.1192/bjp.158.3.317. PMID: 2036528.
91. Salokangas RK. Structure of schizophrenic symptomatology and its changes over time: prospective factor-analytical study. *Acta Psychiatr Scand*. 1997 Jan;95(1):32-9. doi: 10.1111/j.1600-0447.1997.tb00370.x. PMID: 9051158.
92. Salokangas R.K.R., 1999. Symptoms and psychosocial situation in schizophrenia. A prospective follow-up study. *Nord J Psychiatry*. 1999 53; 285–292. <https://doi.org/10.1080/080394899427098>.
93. Salokangas RK. Symptom dimensions and outcome in schizophrenia. *World Psychiatry*. 2003 Oct;2(3):172-8. PMID: 16946931; PMCID: PMC1525103.

94. Kotov R, Foti D, Li K, Bromet EJ, Hajcak G, Ruggero CJ. Validating dimensions of psychosis symptomatology: Neural correlates and 20-year outcomes. *J Abnorm Psychol*. 2016 Nov;125(8):1103-1119. doi: 10.1037/abn0000188. PMID: 27819471; PMCID: PMC5119925.
95. Reininghaus U, Böhnke JR, Chavez-Baldini U, Gibbons R, Ivleva E, Clementz BA, Pearlson GD, Keshavan MS, Sweeney JA, Tamminga CA. Transdiagnostic dimensions of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). *World Psychiatry*. 2019 Feb;18(1):67-76. doi: 10.1002/wps.20607. PMID: 30600629; PMCID: PMC6313235.
96. Toomey R, Kremen WS, Simpson JC, Samson JA, Seidman LJ, Lyons MJ, Faraone SV, Tsuang MT. Revisiting the factor structure for positive and negative symptoms: evidence from a large heterogeneous group of psychiatric patients. *Am J Psychiatry*. 1997 Mar;154(3):371-7. doi: 10.1176/ajp.154.3.371. PMID: 9054785.
97. McGorry PD, Bell RC, Dudgeon PL, Jackson HJ. The dimensional structure of first episode psychosis: an exploratory factor analysis. *Psychol Med*. 1998 Jul;28(4):935-47. doi: 10.1017/s0033291798006771. PMID: 9723148.
98. Tso IF, Taylor SF, Grove TB, Niendam T, Adelsheim S, Auther A, Cornblatt B, Carter CS, Calkins R, Ragland JD, Sale T, McFarlane WR. Factor analysis of the Scale of Prodromal Symptoms: data from the Early Detection and Intervention for the Prevention of Psychosis Program. *Early Interv Psychiatry*. 2017 Feb;11(1):14-22. doi: 10.1111/eip.12209. Epub 2014 Dec 21. PMID: 25529847; PMCID: PMC4723283.
99. Peralta V, Cuesta MJ. Characterization of affective domains within the nonaffective psychotic disorders. *Schizophr Res*. 2009 Jun;111(1-3):61-9. doi: 10.1016/j.schres.2009.03.008. Epub 2009 Mar 24. PMID: 19321311.
100. Liddle PF. The Core Deficit of Classical Schizophrenia: Implications for Predicting the Functional Outcome of Psychotic Illness and Developing Effective Treatments. *Can J Psychiatry*. 2019 Oct;64(10):680-685. doi: 10.1177/0706743719870515. Epub 2019 Aug 21. PMID: 31434513; PMCID: PMC6783668.
101. Strauss GP, Horan WP, Kirkpatrick B, Fischer BA, Keller WR, Miski P, Buchanan RW, Green MF, Carpenter WT Jr. Deconstructing negative symptoms of schizophrenia: avolition-apathy and diminished expression clusters predict clinical presentation and functional outcome. *J Psychiatr Res*. 2013 Jun;47(6):783-90. doi: 10.1016/j.jpsychires.2013.01.015. Epub 2013 Feb 27. PMID: 23453820; PMCID: PMC3686506.
102. Harvey PD, Khan A, Keefe RSE. Using the Positive and Negative Syndrome Scale (PANSS) to Define Different Domains of Negative Symptoms: Prediction of Everyday Functioning by Impairments in Emotional Expression and Emotional Experience. *Innov Clin Neurosci*. 2017 Dec 1;14(11-12):18-22. PMID: 29410933; PMCID: PMC5788247.
103. Roche E, Segurado R, Renwick L, McClenaghan A, Sexton S, Frawley T, Chan CK, Bonar M, Clarke M. Language disturbance and functioning in first episode psychosis. *Psychiatry Res*. 2016 Jan 30;235:29-37. doi: 10.1016/j.psychres.2015.12.008. Epub 2015 Dec 9. PMID: 26699880.
104. Ventura J, Helleman GS, Thames AD, Koellner V, Nuechterlein KH. Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis. *Schizophr Res*. 2009 Sep;113(2-3):189-99. doi: 10.1016/j.schres.2009.03.035. Epub 2009 Jul 22. PMID: 19628375; PMCID: PMC2825750.
105. Cassidy CM, Norman R, Manchanda R, Schmitz N, Malla A. Testing definitions of symptom remission in first-episode psychosis for prediction of functional outcome at 2 years. *Schizophr Bull*. 2010 Sep;36(5):1001-8. doi: 10.1093/schbul/sbp007. Epub 2009 Mar 25. PMID: 19321629; PMCID: PMC2930352.

106. Austin SF, Mors O, Secher RG, Hjorthøj CR, Albert N, Bertelsen M, Jensen H, Jeppesen P, Petersen L, Randers L, Thorup A, Nordentoft M. Predictors of recovery in first episode psychosis: the OPUS cohort at 10 year follow-up. *Schizophr Res.* 2013 Oct;150(1):163-8. doi: 10.1016/j.schres.2013.07.031. Epub 2013 Aug 8. PMID: 23932664.
107. Kwapil TR, Gross GM, Silvia PJ, Barrantes-Vidal N. Prediction of psychopathology and functional impairment by positive and negative schizotypy in the Chapmans' ten-year longitudinal study. *J Abnorm Psychol.* 2013 Aug;122(3):807-15. doi: 10.1037/a0033759. PMID: 24016018.
108. Hegelstad WT, Larsen TK, Auestad B, Evensen J, Haahr U, Joa I, Johannesen JO, Langeveld J, Melle I, Opjordsmoen S, Rossberg JI, Rund BR, Simonsen E, Sundet K, Vaglum P, Friis S, McGlashan T. Long-term follow-up of the TIPS early detection in psychosis study: effects on 10-year outcome. *Am J Psychiatry.* 2012 Apr;169(4):374-80. doi: 10.1176/appi.ajp.2011.11030459. PMID: 22407080.
109. Shibre T, Medhin G, Alem A, Kebede D, Teferra S, Jacobsson L, Kullgren G, Hanlon C, Fekadu A. Long-term clinical course and outcome of schizophrenia in rural Ethiopia: 10-year follow-up of a population-based cohort. *Schizophr Res.* 2015 Feb;161(2-3):414-20. doi: 10.1016/j.schres.2014.10.053. Epub 2014 Nov 22. PMID: 25468171.
110. Ziermans T, de Wit S, Schothorst P, Sprong M, van Engeland H, Kahn R, Durston S. Neurocognitive and clinical predictors of long-term outcome in adolescents at ultra-high risk for psychosis: a 6-year follow-up. *PLoS One.* 2014 Apr 4;9(4):e93994. doi: 10.1371/journal.pone.0093994. PMID: 24705808; PMCID: PMC3976376.
111. Simon AE, Velthorst E, Nieman DH, Linszen D, Umbricht D, de Haan L. Ultra high-risk state for psychosis and non-transition: a systematic review. *Schizophr Res.* 2011 Oct;132(1):8-17. doi: 10.1016/j.schres.2011.07.002. Epub 2011 Jul 23. PMID: 21784618.
112. Schmidt SJ, Schultze-Lutter F, Schimmelmann BG, Maric NP, Salokangas RK, Riecher-Rössler A, van der Gaag M, Meneghelli A, Nordentoft M, Marshall M, Morrison A, Raballo A, Klosterkötter J, Ruhrmann S. EPA guidance on the early intervention in clinical high risk states of psychoses. *Eur Psychiatry.* 2015 Mar;30(3):388-404. doi: 10.1016/j.eurpsy.2015.01.013. Epub 2015 Mar 3. PMID: 25749390.
113. Jordan G, Veru F, Lepage M, Joobor R, Malla A, Iyer SN. Pathways to functional outcomes following a first episode of psychosis: The roles of premorbid adjustment, verbal memory and symptom remission. *Aust N Z J Psychiatry.* 2018 Aug;52(8):793-803. doi: 10.1177/0004867417747401. Epub 2017 Dec 17. PMID: 29250962.
114. Ferraro L, La Cascia C, La Barbera D, Sanchez-Gutierrez T, Tripoli G, Seminerio F, Sartorio C, Marrazzo G, Sideli L, Arango C, Arrojo M, Bernardo M, Bobes J, Del-Ben CM, Gayer-Anderson C, Jongsma HE, Kirkbride JB, Lasalvia A, Tosato S, Llorca PM, Menezes PR, Rutten BP, Santos JL, Sanjuán J, Selten JP, Szöke A, Tarricone I, Muratori R, Tortelli A, Velthorst E, Rodriguez V, Quattrone A, Jones PB, Van Os J, Vassos E, Morgan C, de Haan L, Reininghaus U, Cardno AG, Di Forti M, Murray RM, Quattrone D. The relationship of symptom dimensions with premorbid adjustment and cognitive characteristics at first episode psychosis: Findings from the EU-GEI study. *Schizophr Res.* 2021 Oct;236:69-79. doi: 10.1016/j.schres.2021.08.008. Epub 2021 Aug 14. PMID: 34403965; PMCID: PMC8473991.
115. Paetzold I, Hermans KSFM, Schick A, Nelson B, Velthorst E, Schirmbeck F; EU-GEI High Risk Study; van Os J, Morgan C, van der Gaag M, de Haan L, Valmaggia L, McGuire P, Kempton M, Myin-Germeys I, Reininghaus U. Momentary Manifestations of Negative Symptoms as Predictors of Clinical Outcomes in People at High Risk for Psychosis: Experience Sampling Study. *JMIR Ment Health.* 2021 Nov 19;8(11):e30309. doi: 10.2196/30309. PMID: 34807831; PMCID: PMC8663470.

116. Schlosser DA, Jacobson S, Chen Q, Sugar CA, Niendam TA, Li G, Bearden CE, Cannon TD. Recovery from an at-risk state: clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. *Schizophr Bull.* 2012 Nov;38(6):1225-33. doi: 10.1093/schbul/sbr098. Epub 2011 Aug 8. PMID: 21825282; PMCID: PMC3494042.
117. Salokangas RK, Ruhrmann S, von Reventlow HG, Heinimaa M, Svirskis T, From T, Luutonen S, Juckel G, Linszen D, Dingemans P, Birchwood M, Patterson P, Schultze-Lutter F, Klosterkötter J; EPOS group. Axis I diagnoses and transition to psychosis in clinical high-risk patients EPOS project: prospective follow-up of 245 clinical high-risk outpatients in four countries. *Schizophr Res.* 2012 Jul;138(2-3):192-7. doi: 10.1016/j.schres.2012.03.008. Epub 2012 Mar 31. PMID: 22464922.
118. Fusar-Poli P, Nelson B, Valmaggia L, Yung AR, McGuire PK. Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophr Bull.* 2014 Jan;40(1):120-31. doi: 10.1093/schbul/sbs136. Epub 2012 Nov 22. PMID: 23180756; PMCID: PMC3885287.
119. Falkenberg I, Valmaggia L, Byrnes M, Frascarelli M, Jones C, Rocchetti M, Straube B, Badger S, McGuire P, Fusar-Poli P. Why are help-seeking subjects at ultra-high risk for psychosis help-seeking? *Psychiatry Res.* 2015 Aug 30;228(3):808-15. doi: 10.1016/j.psychres.2015.05.018. Epub 2015 May 30. PMID: 26071897.
120. Rutigliano G, Valmaggia L, Landi P, Frascarelli M, Cappucciati M, Sear V, Rocchetti M, De Micheli A, Jones C, Palombini E, McGuire P, Fusar-Poli P. Persistence or recurrence of non-psychotic comorbid mental disorders associated with 6-year poor functional outcomes in patients at ultra high risk for psychosis. *J Affect Disord.* 2016 Oct;203:101-110. doi: 10.1016/j.jad.2016.05.053. Epub 2016 May 31. PMID: 27285723.
121. Simon AE, Borgwardt S, Riecher-Rössler A, Velthorst E, de Haan L, Fusar-Poli P. Moving beyond transition outcomes: meta-analysis of remission rates in individuals at high clinical risk for psychosis. *Psychiatry Res.* 2013 Oct 30;209(3):266-72. doi: 10.1016/j.psychres.2013.03.004. Epub 2013 Jul 18. PMID: 23871169.
122. McCleery A, Nuechterlein KH. Cognitive impairment in psychotic illness: prevalence, profile of impairment, developmental course, and treatment considerations . *Dialogues Clin Neurosci.* 2019 Sep;21(3):239-248. doi: 10.31887/DCNS.2019.21.3/amccleery. PMID: 31749648; PMCID: PMC6829172.
123. Galderisi S, Rucci P, Kirkpatrick B, Mucci A, Gibertoni D, Rocca P, Rossi A, Bertolino A, Strauss GP, Aguglia E, Bellomo A, Murri MB, Bucci P, Carpiniello B, Comparelli A, Cuomo A, De Berardis D, Dell'Osso L, Di Fabio F, Gelao B, Marchesi C, Monteleone P, Montemagni C, Orsenigo G, Pacitti F, Roncone R, Santonastaso P, Siracusano A, Vignapiano A, Vita A, Zeppegno P, Maj M; Italian Network for Research on Psychoses. Interplay Among Psychopathologic Variables, Personal Resources, Context-Related Factors, and Real-life Functioning in Individuals With Schizophrenia: A Network Analysis. *JAMA Psychiatry.* 2018 Apr 1;75(4):396-404. doi: 10.1001/jamapsychiatry.2017.4607. PMID: 29450447; PMCID: PMC5875306.
124. Ventura J, Subotnik KL, Gretchen-Doorly D, Casaus L, Boucher M, Medalia A, Bell MD, Helleman GS, Nuechterlein KH. Cognitive remediation can improve negative symptoms and social functioning in first-episode schizophrenia: A randomized controlled trial. *Schizophr Res.* 2019 Jan;203:24-31. doi: 10.1016/j.schres.2017.10.005. Epub 2017 Nov 9. PMID: 29128326; PMCID: PMC6589092.
125. Bègue I, Kaiser S, Kirschner M. Pathophysiology of negative symptom dimensions of schizophrenia - Current developments and implications for treatment. *Neurosci Biobehav Rev.* 2020 Sep;116:74-88. doi: 10.1016/j.neubiorev.2020.06.004. Epub 2020 Jun 10. PMID: 32533996.

126. Kahn RS, Sommer IE, Murray RM, Meyer-Lindenberg A, Weinberger DR, Cannon TD, O'Donovan M, Correll CU, Kane JM, van Os J, Insel TR. Schizophrenia. *Nat Rev Dis Primers*. 2015 Nov 12;1:15067. doi: 10.1038/nrdp.2015.67. PMID: 27189524.
127. Rosenheck R, Mueser KT, Sint K, Lin H, Lynde DW, Glynn SM, Robinson DG, Schooler NR, Marcy P, Mohamed S, Kane JM. Supported employment and education in comprehensive, integrated care for first episode psychosis: Effects on work, school, and disability income. *Schizophr Res*. 2017 Apr;182:120-128. doi: 10.1016/j.schres.2016.09.024. Epub 2016 Sep 23. PMID: 27667369.
128. Modini M, Tan L, Brinchmann B, Wang MJ, Killackey E, Glozier N, Mykletun A, Harvey SB. Supported employment for people with severe mental illness: systematic review and meta-analysis of the international evidence. *Br J Psychiatry*. 2016 Jul;209(1):14-22. doi: 10.1192/bjp.bp.115.165092. Epub 2016 Apr 21. PMID: 27103678.
129. Bell MD, Choi KH, Dyer C, Wexler BE. Benefits of cognitive remediation and supported employment for schizophrenia patients with poor community functioning. *Psychiatr Serv*. 2014 Apr 1;65(4):469-75. doi: 10.1176/appi.ps.201200505. PMID: 24382594.
130. Chan JY, Hirai HW, Tsoi KK. Can computer-assisted cognitive remediation improve employment and productivity outcomes of patients with severe mental illness? A meta-analysis of prospective controlled trials. *J Psychiatr Res*. 2015 Sep;68:293-300. doi: 10.1016/j.jpsychires.2015.05.010. Epub 2015 May 21. PMID: 26028551.
131. Albert U, Tomassi S, Maina G, Tosato S. Prevalence of non-psychotic disorders in ultra-high risk individuals and transition to psychosis: A systematic review. *Psychiatry Res*. 2018 Dec;270:1-12. doi: 10.1016/j.psychres.2018.09.028. Epub 2018 Sep 15. PMID: 30243126.
132. Postma MR, van Amelsvoort T, Myin-Germeys I, Gayer-Anderson C, Kempton MJ, Valmaggia L, McGuire P, Murray RM, Garety P, Wykes T, Morgan C, Reininghaus U. Across the continuum: Associations between (fluctuations in) momentary self-esteem and psychotic experiences. *Schizophr Res*. 2021 Dec;238:188-198. doi: 10.1016/j.schres.2021.09.010. Epub 2021 Nov 14. PMID: 34785480.
133. Haijma SV, Van Haren N, Cahn W, Koolschijn PC, Hulshoff Pol HE, Kahn RS. Brain volumes in schizophrenia: a meta-analysis in over 18 000 subjects. *Schizophr Bull*. 2013 Sep;39(5):1129-38. doi: 10.1093/schbul/sbs118. Epub 2012 Oct 5. PMID: 23042112; PMCID: PMC3756785.
134. Hatton SN, Lagopoulos J, Hermens DF, Hickie IB, Scott E, Bennett MR. White matter tractography in early psychosis: clinical and neurocognitive associations. *J Psychiatry Neurosci*. 2014 Nov;39(6):417-27. doi: 10.1503/jpn.130280. PMID: 25111788; PMCID: PMC4214876.
135. Mitelman SA, Newmark RE, Torosjan Y, Chu KW, Brickman AM, Haznedar MM, Hazlett EA, Tang CY, Shihabuddin L, Buchsbaum MS. White matter fractional anisotropy and outcome in schizophrenia. *Schizophr Res*. 2006 Oct;87(1-3):138-59. doi: 10.1016/j.schres.2006.06.016. Epub 2006 Jul 18. PMID: 16854563.
136. Weinberger DR, Aloia MS, Goldberg TE, Berman KF. The frontal lobes and schizophrenia. *J Neuropsychiatry Clin Neurosci*. 1994 Fall;6(4):419-27. doi: 10.1176/jnp.6.4.419. Erratum in: *J Neuropsychiatry Clin Neurosci* 1995 Winter;7(1):121. PMID: 7841813.
137. McGlashan TH, Hoffman RE. Schizophrenia as a disorder of developmentally reduced synaptic connectivity. *Arch Gen Psychiatry*. 2000 Jul;57(7):637-48. doi: 10.1001/archpsyc.57.7.637. PMID: 10891034.

138. Foucher JR, Luck D. Psychosis related to neurological conditions: pro and cons of the dis- / mis-connectivity models of schizophrenia. *Dialogues Clin Neurosci*. 2006;8(1):17-27. doi: 10.31887/DCNS.2006.8.1/jfoucher. PMID: 16640110; PMCID: PMC3181754.
139. Hoffman RE, McGlashan TH. Parallel distributed processing and the emergence of schizophrenic symptoms. *Schizophr Bull*. 1993;19(1):119-40. doi: 10.1093/schbul/19.1.119. PMID: 8451607.
140. Cavelti M, Kircher T, Nagels A, Strik W, Homan P. Is formal thought disorder in schizophrenia related to structural and functional aberrations in the language network? A systematic review of neuroimaging findings. *Schizophr Res*. 2018 Sep;199:2-16. doi: 10.1016/j.schres.2018.02.051. Epub 2018 Mar 3. PMID: 29510928.
141. Foucher JR, Lacambre M, Pham BT, Giersch A, Elliott MA. Low time resolution in schizophrenia Lengthened windows of simultaneity for visual, auditory and bimodal stimuli. *Schizophr Res*. 2007 Dec;97(1-3):118-27. doi: 10.1016/j.schres.2007.08.013. Epub 2007 Sep 19. PMID: 17884350.
142. Rigucci S, Rossi-Espagnet C, Ferracuti S, De Carolis A, Corigliano V, Carducci F, Mancinelli I, Cicone F, Tatarelli R, Bozzao A, Girardi P, Comparelli A. Anatomical substrates of cognitive and clinical dimensions in first episode schizophrenia. *Acta Psychiatr Scand*. 2013 Oct;128(4):261-70. doi: 10.1111/acps.12051. Epub 2012 Dec 9. PMID: 23216145.
143. Bernard JA, Orr JM, Mittal VA. Cerebello-thalamo-cortical networks predict positive symptom progression in individuals at ultra-high risk for psychosis. *Neuroimage Clin*. 2017 Mar 6;14:622-628. doi: 10.1016/j.nicl.2017.03.001. PMID: 28348953; PMCID: PMC5357699.
144. Cao H, Chén OY, Chung Y, Forsyth JK, McEwen SC, Gee DG, Bearden CE, Addington J, Goodyear B, Cadenhead KS, Mirzakhani H, Cornblatt BA, Carrión RE, Mathalon DH, McGlashan TH, Perkins DO, Belger A, Seidman LJ, Thermenos H, Tsuang MT, van Erp TGM, Walker EF, Hamann S, Anticevic A, Woods SW, Cannon TD. Cerebello-thalamo-cortical hyperconnectivity as a state-independent functional neural signature for psychosis prediction and characterization. *Nat Commun*. 2018 Sep 21;9(1):3836. doi: 10.1038/s41467-018-06350-7. PMID: 30242220; PMCID: PMC6155100.
145. Cao H, Ingvar M, Hultman CM, Cannon T. Evidence for cerebello-thalamo-cortical hyperconnectivity as a heritable trait for schizophrenia. *Transl Psychiatry*. 2019 Aug 20;9(1):192. doi: 10.1038/s41398-019-0531-5. PMID: 31431615; PMCID: PMC6702223.
146. Singer MT, Wynne LC. Thought disorder and family relations of schizophrenics. IV. Results and implications. *Arch Gen Psychiatry*. 1965 Feb;12:201-12. doi: 10.1001/archpsyc.1965.01720320089010. PMID: 14237630.
147. Romney DM. Thought disorder in the relatives of schizophrenics. A meta-analytic review of selected published studies. *J Nerv Ment Dis*. 1990 Aug;178(8):481-6. PMID: 2143218.
148. Hietala J, Syvälahti E, Vuorio K, Rökköläinen V, Bergman J, Haaparanta M, Solin O, Kuoppamäki M, Kirvelä O, Ruotsalainen U, et al. Presynaptic dopamine function in striatum of neuroleptic-naive schizophrenic patients. *Lancet*. 1995 Oct 28;346(8983):1130-1. doi: 10.1016/s0140-6736(95)91801-9. PMID: 7475604.
149. Erritzoe D, Talbot P, Frankle WG, Abi-Dargham A. Positron emission tomography and single photon emission CT molecular imaging in schizophrenia. *Neuroimaging Clin N Am*. 2003 Nov;13(4):817-32. doi: 10.1016/s1052-5149(03)00089-3. PMID: 15024964.
150. Uhlhaas PJ, Phillips WA, Silverstein SM. The course and clinical correlates of dysfunctions in visual perceptual organization in schizophrenia during the remission of psychotic symptoms. *Schizophr Res*. 2005 Jun 15;75(2-3):183-92. doi: 10.1016/j.schres.2004.11.005. Epub 2004 Dec 22. PMID: 15885509.

151. Comparelli A, De Carolis A, Corigliano V, Trovini G, Dehning J, Di Pietro S, De Pisa E, Galderisi S, Girardi P. Facial emotion recognition impairment is related to disorganisation in multi-episode schizophrenia. *Schizophr Res Cogn*. 2014 Aug 30;1(2):122-125. doi: 10.1016/j.scog.2014.07.002. PMID: 29379745; PMCID: PMC5779113.
152. Brennan AM, Harris AW, Williams LM. Neural processing of facial expressions of emotion in first onset psychosis. *Psychiatry Res*. 2014 Nov 30;219(3):477-85. doi: 10.1016/j.psychres.2014.06.017. Epub 2014 Jun 18. PMID: 25015712.
153. Jansen van Vuren E, Steyn SF, Brink CB, Möller M, Viljoen FP, Harvey BH. The neuropsychiatric manifestations of COVID-19: Interactions with psychiatric illness and pharmacological treatment. *Biomed Pharmacother*. 2021 Mar;135:111200. doi: 10.1016/j.biopha.2020.111200. Epub 2021 Jan 1. PMID: 33421734; PMCID: PMC7834135.
154. Yazbek H, Norton J, Capdevielle D, Larue A, Boulenger JP, Gély-Nargeot MC, Raffard S. The Lille Apathy Rating Scale (LARS): exploring its psychometric properties in schizophrenia. *Schizophr Res*. 2014 Aug;157(1-3):278-84. doi: 10.1016/j.schres.2014.04.034. Epub 2014 May 27. PMID: 24875172.
155. Kos C, van Tol MJ, Marsman JB, Knegtering H, Aleman A. Neural correlates of apathy in patients with neurodegenerative disorders, acquired brain injury, and psychiatric disorders. *Neurosci Biobehav Rev*. 2016 Oct;69:381-401. doi: 10.1016/j.neubiorev.2016.08.012. Epub 2016 Aug 12. PMID: 27527825.
156. Dwyer DB, Buciuman MO, Ruef A, Kambeitz J, Sen Dong M, Stinson C, Kambeitz-Ilankovic L, Degenhardt F, Sanfelici R, Antonucci LA, Lalouis PA, Wenzel J, Urquijo-Castro MF, Popovic D, Oeztuerk OF, Haas SS, Weiske J, Hauke D, Neufang S, Schmidt-Kraepelin C, Ruhrmann S, Penzel N, Lichtenstein T, Rosen M, Chisholm K, Riecher-Rössler A, Egloff L, Schmidt A, Andreou C, Hietala J, Schirmer T, Romer G, Michel C, Rössler W, Maj C, Borisov O, Krawitz PM, Falkai P, Pantelis C, Lencer R, Bertolino A, Borgwardt S, Noethen M, Brambilla P, Schultze-Lutter F, Meisenzahl E, Wood SJ, Davatzikos C, Uptegrove R, Salokangas RKR, Koutsouleris N; PRONIA Consortium. Clinical, Brain, and Multilevel Clustering in Early Psychosis and Affective Stages. *JAMA Psychiatry*. 2022 Jul 1;79(7):677-689. doi: 10.1001/jamapsychiatry.2022.1163. PMID: 35583903; PMCID: PMC9118078.
157. Correll CU, Schooler NR. Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. *Neuropsychiatr Dis Treat*. 2020 Feb 21;16:519-534. doi: 10.2147/NDT.S225643. PMID: 32110026; PMCID: PMC7041437.
158. Bortolon C, Macgregor A, Capdevielle D, Raffard S. Apathy in schizophrenia: A review of neuropsychological and neuroanatomical studies. *Neuropsychologia*. 2018 Sep;118(Pt B):22-33. doi: 10.1016/j.neuropsychologia.2017.09.033. Epub 2017 Sep 28. PMID: 28966139.
159. Mørch-Johnsen L, Agartz I, Jensen J. The Neural Correlates of Negative Symptoms in Schizophrenia: Examples From MRI Literature. *Clin EEG Neurosci*. 2018 Jan;49(1):12-17. doi: 10.1177/1550059417746214. PMID: 29243527.
160. Kirschner M, Hager OM, Bischof M, Hartmann MN, Kluge A, Seifritz E, Tobler PN, Kaiser S. Ventral striatal hypoactivation is associated with apathy but not diminished expression in patients with schizophrenia. *J Psychiatry Neurosci*. 2016 Apr;41(3):152-61. doi: 10.1503/jpn.140383. Erratum in: *J Psychiatry Neurosci*. 2017 Mar;42(2):102. PMID: 26395814; PMCID: PMC4853206.
161. Amodio A, Quarantelli M, Mucci A, Prinster A, Soricelli A, Vignapiano A, Giordano GM, Merlotti E, Nicita A, Galderisi S. Avolition-Apathy and White Matter Connectivity in Schizophrenia: Reduced Fractional Anisotropy Between Amygdala and Insular Cortex. *Clin EEG Neurosci*. 2018 Jan;49(1):55-65. doi: 10.1177/1550059417745934. PMID: 29243529.

162. Bègue I, Kaiser S, Kirschner M. Pathophysiology of negative symptom dimensions of schizophrenia - Current developments and implications for treatment. *Neurosci Biobehav Rev.* 2020 Sep;116:74-88. doi: 10.1016/j.neubiorev.2020.06.004. Epub 2020 Jun 10. PMID: 32533996.
163. Kirschner M, Schmidt A, Hodzic-Santor B, Burrer A, Manoliu A, Zeighami Y, Yau Y, Abbasi N, Maatz A, Habermeyer B, Abivardi A, Avram M, Brandl F, Sorg C, Homan P, Riecher-Rössler A, Borgwardt S, Seifritz E, Dagher A, Kaiser S. Orbitofrontal-Striatal Structural Alterations Linked to Negative Symptoms at Different Stages of the Schizophrenia Spectrum. *Schizophr Bull.* 2020 Dec 1:sbaa169. doi: 10.1093/schbul/sbaa169. Epub ahead of print. PMID: 33257954.
164. Wang X, Lu F, Duan X, Han S, Guo X, Yang M, Zhang Y, Xiao J, Sheng W, Zhao J, Chen H. Frontal white matter abnormalities reveal the pathological basis underlying negative symptoms in antipsychotic-naïve, first-episode patients with adolescent-onset schizophrenia: Evidence from multimodal brain imaging. *Schizophr Res.* 2020 Aug;222:258-266. doi: 10.1016/j.schres.2020.05.039. Epub 2020 May 24. PMID: 32461088.
165. Veerman SRT, Schulte PFJ, de Haan L. Treatment for Negative Symptoms in Schizophrenia: A Comprehensive Review. *Drugs.* 2017 Sep;77(13):1423-1459. doi: 10.1007/s40265-017-0789-y. PMID: 28776162.
166. Jones MT, Strassnig MT, Harvey PD. Emerging 5-HT receptor antagonists for the treatment of Schizophrenia. *Expert Opin Emerg Drugs.* 2020 Jun;25(2):189-200. doi: 10.1080/14728214.2020.1773792. Epub 2020 Jun 8. PMID: 32449404.
167. Stahl SM, Lee-Zimmerman C, Cartwright S, Morrissette DA. Serotonergic drugs for depression and beyond. *Curr Drug Targets.* 2013 May 1;14(5):578-85. doi: 10.2174/1389450111314050007. PMID: 23531115.
168. Vidal C, Reese C, Fischer BA, Chiapelli J, Himelhoch S. Meta-Analysis of Efficacy of Mirtazapine as an Adjunctive Treatment of Negative Symptoms in Schizophrenia. *Clin Schizophr Relat Psychoses.* 2015 Summer;9(2):88-95. doi: 10.3371/CSRP.VIRE.030813. Epub 2013 Mar 14. PMID: 23491969.
169. Harvey PD, Saoud JB, Luthringer R, Moroz S, Blazhevych Y, Stefanescu C, Davidson M. Effects of Roluperidone (MIN-101) on two dimensions of the negative symptoms factor score: Reduced emotional experience and reduced emotional expression. *Schizophr Res.* 2020 Jan;215:352-356. doi: 10.1016/j.schres.2019.08.029. Epub 2019 Sep 2. PMID: 31488314.
170. Strauss GP, Zamani Esfahlani F, Sayama H, Kirkpatrick B, Opler MG, Saoud JB, Davidson M, Luthringer R. Network Analysis Indicates That Avolition Is the Most Central Domain for the Successful Treatment of Negative Symptoms: Evidence From the Roluperidone Randomized Clinical Trial. *Schizophr Bull.* 2020 Jul 8;46(4):964-970. doi: 10.1093/schbul/sbz141. PMID: 31989151; PMCID: PMC7342174.
171. Austin SF, Mors O, Secher RG, Hjorthøj CR, Albert N, Bertelsen M, Jensen H, Jeppesen P, Petersen L, Randers L, Thorup A, Nordentoft M. Predictors of recovery in first episode psychosis: the OPUS cohort at 10 year follow-up. *Schizophr Res.* 2013 Oct;150(1):163-8. doi: 10.1016/j.schres.2013.07.031. Epub 2013 Aug 8. PMID: 23932664.



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REPRESENTATIVENESS OF CLINICAL ANTIPSYCHOTIC TRIAL SAMPLES WHEN COMPARED WITH A GENERAL POPULATION-BASED SAMPLE

ABSTRACT

Background: Antipsychotics are effective in controlled environments for treatment of schizophrenia. However, there is hardly any research on the effects of antipsychotics in years-long follow-ups in antipsychotic trials. In addition, study samples of the antipsychotic trials differ quite notably from the day-to-day clinical treatment population. In this study, we aimed to compare the population-based Northern Finland Birth Cohort 1966 (NFBC1966) population to the samples in antipsychotic trials using typical inclusion and exclusion criteria found in randomized clinical trials (RCTs). We also compared long-term outcomes of individuals with schizophrenia meeting and not meeting inclusion criteria for clinical trials.

Method: We gathered clinical antipsychotic trials and their inclusion and exclusion criteria. These inclusion and exclusion criteria were compared to the data of NFBC1966 to find out how many of the 54 participants in NFBC1966 34-year follow-up would meet these criteria, and how representative outcomes of the clinical antipsychotic trials are compared to a longitudinal population-based sample.

Result: Depending on how strict the inclusion and exclusion criteria of the RCTs were, 10.5 to 24.6 per cent of the participants in the NFBC1966 34-year follow-up could have been included in RCTs using the criteria. Notably, 42.1 per cent of the participants in the NFBC1966 would be excluded without considering PANSS as inclusion criteria. There was no statistically significant difference in the distribution of PANSS and SOFAS scores between the included and excluded groups in longitudinal analysis. However, in the distribution of hospital treatment days in the groups included and excluded by criteria of RCTs, there was a statistically significant difference between the groups.

Conclusions: Over one-third of the participants of this population sample could have been excluded from clinical trials without even considering psychotic symptoms as an inclusion criterion.

KEYWORDS: SCHIZOPHRENIA, ANTIPSYCHOTIC TRIALS, POPULATION-BASED, REPRESENTATIVENESS,
INCLUSION AND EXCLUSION CRITERIA

INTRODUCTION

Schizophrenia is globally seen as one of the most serious and disabling mental illnesses, where the early starting age of the disease and the severe symptoms often lead to severe effects on day-to-day life and performance. The global prevalence of the disease is estimated to be slightly less than one per cent, and in Finland, it is estimated to be around one per cent, which means around 50 000 individuals with schizophrenia in Finland[1]. The baseline for treatment of schizophrenia is early recognition of the disease, a long-sustained care relationship and personalized care planning, which often includes of the use of antipsychotic medications [2,3].

Antipsychotics, especially long-acting injections, are proven to be effective in controlled environments for positive symptoms and prevent recurrence after remission [4,5]. However, there is hardly any research about antipsychotics' effect on negative symptoms and adverse effects in years-long follow-ups. According to Leucht et al., in 65 randomized controlled trials (RCTs), the median duration of follow-up was 26 weeks and there were only a few 3-year follow-ups [6].

The essential difference between samples in antipsychotic RCTs and patient material in the clinical real world is the relatively narrow inclusion and exclusion criteria in RCTs. Clinical drug trials' inclusion and exclusion criteria are meant to confirm that patient material is homogeneous, and that the tested drug is used on an individual who has the disease meant for the medicine in question. Inclusion and exclusion criteria are used to select patients whose disease is severe enough, but not so severe that there would not be any expected positive outcome. Therefore, the selection of patient material in clinical trials may differ greatly from clinical patient material. The psychiatric conditions of patients in clinical trials of mental illnesses are milder than in ordinary clinical patient material. In addition, comorbidities are more often met with clinical real-world patients, and in some cases patients' daily function is much worse compared with individuals in clinical drug trials. When comparing randomized controlled trials to the clinical world, the difference between efficacy and effectiveness has to be noted [7].

The differences between RCTs and the clinical real-world patient samples are also acknowledged in the terminology of the effect of medications, for example, antipsychotics. Efficacy is defined as an expected end result under ideal circumstances, for example, in RCT designs, and the effectiveness indicates effects in a more realistic setup with more interfering factors in the real-world population [8].

In this study, the aim was to compare the characteristics of persons with schizophrenia in a general population sample to inclusion and exclusion criteria of clinical antipsychotic trials. The general population sample was drawn from the Northern Finland Birth Cohort 1966 (NFBC1966). As Kennedy-Martin et al. [7] predicts and as a hypothesis for this study, we assume that individuals with schizophrenia in the NFBC1966 are more severely ill and have more comorbidities than the clinical antipsychotic trial material. Accordingly, it is also assumed that only a small part of the NFBC1966 population with schizophrenia could be included in an average clinical antipsychotic trial. We also aimed to compare the outcome of this presumably small population of individuals meeting the inclusion and exclusion criteria to the population not meeting the criteria.

NFBC1966 has been active on schizophrenia for over 30 years. During that time, the longitudinal research has allowed various risk factors to be found, for example, parental psychosis and delays in normal growth in the early stages of childhood [9]. Because of the wide variety of outcomes and general heterogeneity of schizophrenia as a disease, there has been meaningful study on predictors for different outcomes of the disease, even the use of antipsychotics as a predictor. For example, according to Moilanen et al. [10], cumulative high dosage and long-term use of antipsychotics, especially polypharmacy, was associated with unfavourable outcomes, and steady low dosage use was more favourable.

MATERIAL AND METHODS

THE NORTHERN FINLAND BIRTH COHORT 1966

The Northern Finland Birth Cohort 1966 (NFBC1966) is a longitudinal population-based sample, with collection having begun during the antenatal period of the participants. It includes 96 per cent of individuals (12 058 liveborn) that were expected to be born in 1966 in the area of Northern Finland [11,12]. NFBC1966 differs from randomized controlled trials (RCT), especially in the way persons with schizophrenia are involved in the sample. People affected by schizophrenia are not involved via healthcare or drug trial, they are involved as an individual in a part of cohort research and involved as a part of schizophrenia research via several nationwide registers.

During the years 1999 to 2001, a 34-year follow-up was performed in the NFBC1966. Individuals who had had a psychotic episode by the year 1997 were invited

to participate. Altogether 91 individuals with psychosis, of which 61 had a schizophrenia diagnosis, participated. Participants were imaged with MRI and interviewed with questions of, for example, use of antipsychotics, symptoms, somatic diseases and substance abuse. Based on the interview, different assessments, for example, Positive and Negative Syndrome Scale (PANSS), Clinical Global Index (CGI) and Social Occupational Functioning Assessment Scale (SOFAS) were conducted. During the years 2008 to 2010, a new follow-up at the age of 43 years was carried out. The 43-year follow-up also included 107 individuals who had had a psychotic disorder between the years 1998 and 2008, of which 54 were with schizophrenia. The research protocol was the same as outlined. Altogether 40 individuals with schizophrenia attended both the 34-year follow-up and the 43-year follow-up. Four of these individuals left the cohort study making the total participants of both studies 36[10].

GATHERING AND EVALUATION OF THE INCLUSION AND EXCLUSION CRITERIA IN THE CLINICAL TRIALS

To map out the representativeness of individuals in antipsychotic trials, recent meta-analyses of antipsychotic trials of schizophrenia were evaluated. Based on representativeness and the minor number of first-episode studies, we chose two meta-analyses by Leucht et al. [13,14]. Leucht et al. (2013) included 212 trials between 1955 and 2012, and Leucht et al. (2017) included 167 trials between 1955 and 2016. According to the names of the authors, publication year and the description of the original study, there were 77 studies that were included in both the 2013 and 2017 meta-analyses. The number may not be totally accurate, because Leucht et al. (2013) cites only 203 of the 212 trials because some publications reported on two or more studies. The original articles of the meta-analyses were read and the inclusion and exclusion criteria for the studies were collected. At this point, the studies that we could not access full text via the library of the University of Oulu were ruled out. Also, studies that could not be compared to NFBC1966, for example, studies considering only first onset of psychosis, were excluded. The studies and their inclusion and exclusion criteria were systematically collected from newest study to oldest until the most common ones had repeated themselves and saturated to stand out (until the year 2010). The total amount of original studies was 22, which is around 7 per cent of the total amount of studies included in Leucht et al. 2013 and 2017.

STATISTICAL METHODS

In cross-tabulations, percentages and Chi-Square tests (Pearson Chi-Square and Fisher's Exact test) were used to evaluate findings. The mean, median, standard deviation and range were used to describe continuous variables, and statistical differences were tested with the Mann-Whitney U test. Also, cumulative hospital treatment days (from national Care Register of Health Care) were analysed in both included and excluded groups using the same inclusion and exclusion criteria. IBM SPSS Statistics version 27 was used for the analyses.

RESULTS

MOST COMMON INCLUSION AND EXCLUSION CRITERIA IN THE CLINICAL TRIALS OF ANTIPSYCHOTICS

The 22 original studies were read systematically, tabulating all inclusion and exclusion criteria in the articles themselves or in the attachments. Due to the individual lexical formulation of the criteria in each study, differently worded but with the same meaning, criteria were combined so they retained their representativeness. The most often used inclusion and exclusion criteria were tabulated as seen in *Table 1*. Inclusion criteria often held diagnostic instruments (for example, PANSS and CGI) to map out the severity of the disease and symptoms and whether the study included inpatients or outpatients. Exclusion criteria often held restrictions on the antipsychotics individuals had been using earlier, how the individual's disease had reacted to earlier treatments and comorbidities.

Positive and Negative Syndrome Scale (PANSS)

Positive and Negative Syndrome Scale (PANSS) is a scale used to evaluate the severity of symptoms of individuals with psychosis. The PANSS score ranges from 30 to a maximum of 210 points[12]. In any form, PANSS was mentioned in 19 original studies. The score used to include and exclude individuals ranged from 42 to a maximum of 120 points, most commonly around 70 to 80 points. In 11 of the 22 original studies, the authors also required at least 4 points in at least two items in the positive subscale of the PANSS. Three of the original studies, which did not use PANSS as inclusion criteria, used Brief Psychiatric Rating Scale (BPRS) instead of PANSS.

Table 1. Most common inclusion and exclusion criteria in the original studies of Leucht et al. meta-analyses (13, 14)

Original study	PANNS as inclusion criteria	CGI ≥ 4 as inclusion criteria	Hospitalization as inclusion criteria	History of poor response to antipsychotics and earlier antipsychotic treatment	Other psychiatric diseases	Major somatic diseases
Correl et al. 2016	no	no	yes	no	excluded	No
Kinoshita et al. 2016	total ≥ 60 + pos. subscale criteria	yes	yes	excluded	no	No
Liebermann et al. 2016	no	no	no	excluded	excluded	excluded
Litman et al. 2016	total ≥ 70	yes	no	excluded	excluded	No
Loebel et al. 2016.	total ≥ 80 + pos. subscale criteria	no	yes	no	excluded	no
Correl et al. 2015	no	yes	yes	no	excluded	no
Kane et al. 2015	no	yes	yes	no	excluded	no
Durgam et al. 2014	total 80-120 + pos. subscale criteria	yes	yes	excluded	excluded	no
Bugarski-Kriola et al. 2014	total 80-120 + pos. subscale criteria	yes	yes	excluded	no	no
Downing et al. 2014	no	yes	yes	excluded	excluded	excluded
Litmann et al. 2014	total ≥ 70	no	no	excluded	excluded	no
Shen et al. 2014	total 70-120 + pos. subscale criteria	yes	yes	excluded	excluded	no
Egen et al. 2013	total ≥ 70 + pos. subscale criteria	no	no	excluded	excluded	excluded
Loebel et al. 2013	total ≥ 80 + pos. subscale criteria	yes	yes	no	no	no
Nasrallah et al. 2013	total ≥ 80 + pos. subscale criteria	yes	yes	excluded	excluded	excluded



Original study	PANNS as inclusion criteria	CGI ≥ 4 as inclusion criteria	Hospitalization as inclusion criteria	History of poor response to antipsychotics and earlier antipsychotic treatment	Other psychiatric diseases	Major somatic diseases
Ogasa et al. 2012	total ≥ 42 + pos. subscale criteria	yes	yes	excluded	excluded	excluded
Schmid et al. 2012	total 60-120	yes	yes	excluded	excluded	excluded
Coppola et al. 2011	total 70-120	yes	yes	excluded	excluded	excluded
Ghaleiha et al. 2011	total ≥ 60	yes	yes	excluded	excluded	excluded
Kinon et al. 2011	no	yes	yes	excluded	no	excluded
Meltzer et al. 2011	total ≥ 80 + pos. subscale criteria	yes	yes	excluded	no	no
Kane et al. 2010	total ≥ 60	yes	yes	no	excluded	excluded

Clinical Global Impression Scale (CGI)

Clinical Global Impression Scale (CGI) is a 7-point scale to measure illnesses severity ranging from “not mentally ill” to “among the most severely ill”. CGI was mentioned in 13 of 22 original studies with scores restricted to at least or greater than 4 in all of them, meaning the individuals who were at least moderately ill. There was no mention of the maximum CGI score in the original studies.

Hospitalization

As well as hospitalization, acute exacerbation was a common inclusion criterion in the original studies, in fact, it was mentioned in 20 of the 22 original studies. Because of the nature of the NFBC1966, acute exacerbation could not be used as a variable and was excluded from the collected inclusion and exclusion criteria of the original studies. However, as a common guideline for the treatment of acute exacerbation of schizophrenia, hospitalization often follows acute exacerbation to manage and control relapsed disease and the possible changes in patients’ use of antipsychotics. 18 of the 22 original studies mention hospitalization as an inclusion criterion. Six of the original studies were more

specific on the length of the hospitalization and four of the studies were completed with the patients being outpatients.

History of poor response to antipsychotics and earlier antipsychotic treatment

Due to individual vocabulary in the original studies, the combined “history of poor response to antipsychotics” criteria, consists of often mentioned “must have history of positive response to antipsychotics” in any form, diagnostic criteria of treatment-resistant schizophrenia (at least 2 different antipsychotics with adequate dosage and time) and the plain use of clozapine. In some way, history of poor response to antipsychotics is mentioned in 12 of the 22 original studies.

In total, eight of the original studies had restricted the use of certain antipsychotics before the trial with or without the history of poor response mentioned. Most commonly the case was depot antipsychotics during a certain timeline before the baseline. Break from the depot antipsychotics was mentioned as an inclusion criterion in four original studies and the break required before the baseline or the study ranged from 1 cycle of mentioned depot antipsychotics to 120 days.

Other psychiatric disorders

Psychiatric DSM-IV Axis I diagnosis other than schizophrenia was mentioned as an exclusion criterion in 17 of the 22 original studies. Nine of the studies excluded all diagnoses other than schizophrenia in the Axis I, three ruled out schizoaffective disorder, three ruled out major depression and two ruled out bipolar disorders.

DSMV-IV Axis I also contains diagnoses for substance abuse. In 13 original studies, substance abuse and/or dependence is mentioned as its own exclusion criteria. Six of the original studies do not mention any specific timeline, 5 studies exclude participants for substance abuse within 180 days before trial and 2 for 3 months before screening.

Somatic diseases

Major somatic diseases are characterized in some of the original studies as acute, unstable or untreated somatic diseases. Eight of the 22 original studies excluded individuals with any significant medical condition other than schizophrenia. Also, three of the 22 studies excluded participants with clinically significant abnormal laboratory values.

Chronic diseases of the central nervous system were mentioned in 10 of the 22 original studies. Two of these studies excluded any chronic central nervous system disease, but, for example, dementia, seizures and epilepsy were specifically mentioned

SELECTED INCLUSION AND EXCLUSION CRITERIA FROM THE ORIGINAL STUDIES IN THE NFBC1966 34-YEAR FOLLOW-UP

Positive and negative syndrome scale (PANSS)

Total PANSS score was available from 54 participants with a mean of 55.2 and a median of 50.1, ranging from a minimum of 30 to a maximum of 122. Altogether, 17 participants (31.5 per cent) had a total PANSS score of at least 60 and 11 participants (20.4 per cent) had a PANSS total of at least 60 with at least moderate severity in two or more of the positive symptoms. When total PANSS is restricted to at least 70, 10 participants (18.5 per cent) would be included, and when at least two moderate positive symptoms are counted in, seven participants (13.0 per cent) would be included.

Positive PANSS scores were also evaluated from the 54 participants. The mean was 13.70 (SD 5.19) ranging from 7 to 24 with a median of 13.5.

Table 2. The number of included participants by different Positive and Negative Syndrome (PANSS) inclusion criteria in the population of NFBC1966 34-year follow-up (N=54)

PANSS as an inclusion criterion 34y	N (%)
Total PANSS at least 60	17 (31.5)
Total PANSS at least 60 and at least 2 positive symptoms at least moderate severity	11 (20.4)
Total PANSS at least 70	10 (18.5)
Total PANSS at least 70 and at least 2 positive symptoms at least moderate severity	7 (13.0)

Clinical Global Impression Scale (CGI)

Clinical Global Impression Scale is available from a total of 57 participants in NFBC1966. Altogether, 51 participants (89.5 per cent) had a CGI score of at least moderate severity (CGI score of at least four).

Hospitalization

Because of the nature of the NFBC1966, there is no data from acute exacerbation of the participants with schizophrenia. However, there is cumulative data on days spent in hospital treatment which may indirectly suggest the commonness of both acute exacerbation and hospitalization. The cumulative hospital treatment days were collected from inpatients in the timeline 1.1.2000 to 31.12.2009.

History of poor response to antipsychotics and earlier antipsychotic treatment

Treatment resistant is considered in the NFBC1966 to be the use of clozapine or the use of at least two different antipsychotics with the dose of 600 chlorpromazine (CPZ). At the 34-year follow-up, 13 of the 56 participants (23.2 per cent) with available medical therapy history were considered treatment resistant at some point of their disease.

Other psychiatric diseases

During the 34-year follow-up, 6 of the 57 participants (10.5 per cent) had a psychiatric diagnosis other than schizophrenia. Also, 5 of the 57 participants (8.8 per cent) had a current substance abuse diagnosis.

Somatic diseases

In the 34-year follow-up of NFBC1966, 5 of the 55 total (9.1 per cent) participants were considered to have a major somatic disorder.

INCLUSION AND EXCLUSION CRITERIA OF THE ORIGINAL STUDIES COMPARED WITH THE POPULATION OF NFBC1966

In this study, we aimed to compare the population of the NFBC1966 with the population used in antipsychotic trials. After searching through inclusion and the exclusion criteria of the 22 original studies, we managed to make an estimated combination of the criteria used in antipsychotic trials. This combination includes PANSS as inclusion criteria set on different scores according to the commonness in the original studies. The combination uses CGI, treatment-resistant schizophrenia (TRS), current substance abuse and major somatic diseases as exclusion criteria. Hospitalization was not included, because of the longitudinal nature of the NFBC1966.

Combined exclusion criteria in NFBC1966 in the 34-year follow-up

Combined exclusion criteria consist of CGI less than moderate, individuals with treatment-resistant schizophrenia, current substance abuse or major somatic disorder. Twenty-four of the 57 individuals (42.1 per cent) would be excluded, and the remaining 33 individuals could be included depending on their PANSS score. PANSS was then accounted to the combined exclusion criteria in different scales which appeared the most often during the collection of the exclusion criteria of the original studies.

When comparing the combined inclusion and exclusion criteria to the inclusion criteria shown in *Table 2*, three additional participants would be excluded by the combined exclusion criteria in the group who had a PANSS total score of at least 60, two in the group with a PANSS total score at least 60 and the positive subscale counted in, two in the group with PANSS total at least 70, and one participant would be excluded in the group with total PANSS at least 70 and the positive subscale counted in.

For the individuals who would be excluded by the combination criteria, the mean for hospital treatment days from 1.1.2000 to 31.12.2009 caused by any psychosis was 164.88 with a standard deviation of 250.21 (N=43). Individuals who would be included had a mean of 30.86 days with a standard deviation of 44.55 (N=14). There was a statistically significant difference between the included and excluded groups in the Mann-Whitney U test (p-value 0.041).

Table 3. Different PANSS criteria with combined exclusion criteria (CGI less than moderate, individuals with treatment-resistant schizophrenia, current substance abuse, or major somatic disorder) of the original studies in NFBC1966 34-year follow-up
PANSS = Positive and Negative Scale

Combined exclusion criteria and different PANSS criteria	Included (%)	Excluded (%)	Total (%)
Total PANSS at least 60	14 (24.6%)	43 (75.4%)	57 (100%)
Total PANSS at least 60 and at least two moderate symptoms on positive subscale	9 (15.8%)	48 (84.2%)	57 (100%)
Total PANSS at least 70	8 (14.0%)	49 (86.0%)	57 (100%)
Total PANSS at least 70 and at least moderate symptoms on positive subscale	6 (10.5)	49 (89.5%)	57 (100%)

Table 4. Cumulative hospital treatment days caused by any psychosis from 1.1.2000 to 31.12.2009 in NFBC1996 individuals with schizophrenia divided into inclusion and exclusion groups by combination criteria of PANNS at least 60, CGI at least 4, and exclusion criteria of TRS, current substance abuse, other psychiatric and major somatic diseases

Combination criteria		Any psychosis hospital treatment days
Excluded	Mean	164.88
	SD	250.21
	N	43
Included	Mean	30,86
	SD	44.55
	N	14
Total	Mean	131.96
	SD	225.40
	N	57

Combined exclusion criteria in NFBC1966 in the 43-year follow up

NFBC1966 is longitudinal research, and the participants that attended the 34-year follow-up in the years 1999 to 2001 were also asked to attend the 43-year follow-up during the years 2008 to 2010. There had been some loss of participants, which affects the data based on the voluntary attending for the research. There is data from 36 participants who were evaluated in both the 34-year follow-up and in the 43-year follow-up.

Using the same combined exclusion criteria, at the 43-year follow-up, 20 individuals of 36 available participants (55.6 per cent) could be included. In this population, total PANSS had a mean of 72.5 and a median of 72 ranging from 30 to 130. With the individuals who would be excluded, the total PANSS had a mean of 83.4 and a median of 90.5 ranging from 39 to 131.

When using PANSS >70 as an inclusion criterion with the combined exclusion criteria, 10 participants of the 36 individuals (27.8 per cent) could be included. Using Pearson

Chi-Square, there was no statistically significant difference between the groups (p=0.453). When the PANSS total was divided into groups >60 and 60 or lower, the group size of the participants, who would have been excluded and had a PANSS total of 60 or lower, was so small that the analysis prevented the use of an exact number of individuals because of restriction of privacy. However, using Fisher’s Exact Test, there was no statistical significance in the difference between the groups of PANSS total >60 and 60 or lower (p=0.718).

Comparing the inclusion and exclusion criteria results between 34-year follow-up and 43-year follow-up

Because the unavailable data of 43-year follow-up group divided by total PANSS >60 and 60 or less, we chose the cutting point of groups as PANSS at least 70. Participants in the 34-year follow-up, who had PANSS total score of at least 70 were included and exclusions were made with the same combination criteria which were used earlier, which were analysed in the 43-year follow-up as seen in [Table 5](#).

Table 5. Combination criteria (CGI <4, TRS, current substance abuse, and major somatic diseases), in the 43-year follow-up population

Excluded by combination criteria									
Outcome at 43 years	Yes			No			Total		
	N	Mean (SD)	Median	N	Mean (SD)	Median	N	Mean (SD)	Median
PANSS total score	16	83.44 (28.58)	90.50	20	72.55 (25.61)	72.00	36	77.39 (27.14)	75.50
PANSS positive symptoms score	16	18.50 (7.68)	18.50	20	15.10 (5.57)	16.50	36	16.61 (6.71)	17.00
SOFAS	16	44.69 (18.64)	34.50	20	49.10 (13.33)	47.00	36	47.14 (15.82)	43.50

Table 6. Participants were evaluated during the 34-year follow-up and grouped with the inclusion and exclusion criteria of the original studies compared with their evaluation in the 43-year follow-up

PANSS at least 70 and combination exclusion criteria in 34y		PANSS total in 43y	PANSS positive symptoms score in 43y	SOFAS in 43y
Excluded	Mean	75.84	17.00	48.32
	Median	74.00	17.00	45.00
	N	31	31	31
	Standard deviation	27.54	7.06	16.160
Included	Mean	87.00	14.20	39.80
	Median	79.00	16.00	37.00
	N	5	5	5
	Standard deviation	24.92	3.42	12.40
Total	Mean	77.39	16.61	47.14
	Median	75.50	17.00	43.50
	N	36	36	36
	Standard deviation	27.14	6.712	15.82

In the follow-up of both excluded and included groups in the 34-year follow-up, there was no statistically significant difference (Mann-Whitney U test) in the distribution of PANSS, positive or negative score or SOFAS in the 34-year follow-up groups of the combination criteria (p-value ranging from 0.325 to 0.396). The analysis was the same when PANSS score >70 was removed from the combination criteria.

DISCUSSION

Variation between clinical antipsychotic samples and natural population-based samples is caused by inclusion and exclusion criteria and the overall homogeneity of the sample, which is needed in RCTs. However, in the clinical world, patients are different, and heterogeneity is normal. The differences between our samples are quite significant.

Depending on how strict the criteria for including and excluding individuals were used, 75.4 to 89.5 per cent of the NFBC1966 would not be included in clinical antipsychotic trials, and the results of the trials would not be necessarily generalizable to the NFBC sample. However, the statistical analyses showed no statistically significant difference between the included and excluded groups when only the inclusion and exclusion variables were compared. A statistically significant difference was found in long-term outcomes between the included and excluded groups. Taipale et al. (2022) estimated that RCTs may represent only about a fifth of the individuals with schizophrenia spectrum disorders in a population-based cohort with a total of 20 060 individuals with schizophrenia. Our findings follow the estimate on a smaller scale. However, in Taipale et al. [15] they simply used exclusion criteria to compare individuals, and in our study, we also used factors that are

used as inclusion criteria in clinical trials. Taipale et al. were more specific and went further in the identification of the exclusion criteria than we did in our study, and in our study, the criteria for exclusion had much weight in PANSS symptoms. The end results in our study and in Taipale et al. were in the same range but for different reasons.

The reason for the difference between the RCTs population and population-based data can probably be divided into two. First is the selection of the RCTs population to maximize the possibility of efficacy while the NFBC1966 population is natural and unselected. The second reason is that most of the participants in NFBC1966 were currently outpatients without acute exacerbation, while the individuals in the collected RCTs were included during the acute exacerbation of the disease, which has an effect, especially in PANSS scores. There would be a benefit in examining cohort studies as well, with RCTs of antipsychotics used for relapse prevention to map out further differences between selected and unselected individuals with schizophrenia. However, in the clinical mind, our finding is still notable. Both groups are treated with the same medicines (with different dosages), but the findings based on the use of those medicines are collected with acutely more severely ill individuals with fewer factors that may affect the outcome of treatment. There is not too much research on antipsychotics and their outcomes with unselected participants and the adverse effects of antipsychotics in years-long follow-ups. Our findings let us guess that there could be major differences in both if they were later studied.

During the years of NFBC1966 schizophrenia research, there have been studies informing the outcomes of individuals with schizophrenia. In Lauronen et al. [16], they used PANSS positive symptoms as a criterion for outcome. As a part of describing poor clinical outcome, an individual should have had more than one moderate positive symptom counting delusions, conceptual disorganization and hallucinations. In the original studies' inclusion criteria collected for this study, PANSS with at least two moderate positive symptoms was often mentioned. As a naturalistic setup (NFBC1966) and the fact that these individuals already had started treatment, this group included with the criteria of at least two moderate positive symptoms would automatically be a part of the poor outcome group depending on if the two moderate ones consisted of the three mentioned above. However, when only the PANSS total score (restricted to at least 70) was noted in the 34-year follow-up, when analysed, the same individuals were again in the 43-year follow-up, the included individuals in the 34-year follow-up had fewer positive symptoms score

in the 43-year follow-up than the individuals excluded. This may indirectly suggest that the included individuals in the 34-year follow-up may have had a better prognosis than the individuals excluded, however, more research would be needed to confirm this. An important aspect for following studies would be to study differences in mortality rates between the included and excluded groups.

In the clinical world, the difference in outcomes between clinical antipsychotic trials and in the real-world population has to be noted. If the clinical antipsychotic trials represent only around 25 per cent of the clinical world population as our findings suggest, the same outcomes cannot be expected in both groups. This further highlights the need for systematic medication management for individuals with schizophrenia, as the same antipsychotics are used as a long-term treatment to prevent relapses in schizophrenia.

LIMITATIONS AND STRENGTHS

The main limitation of this study is the rather small size of the NFBC1966 sample and loss of the participants during the follow-up. NFBC1966 is a naturalistic study of individuals expected to be born in 1966 and the number of individuals with a schizophrenia diagnosis is restricted by this. In the 34-year follow-up, there were 57 individuals with a schizophrenia diagnosis, and 36 of them were evaluated again in the 43-year follow-up. The loss of participants has been studied in the NFBC1966. Haapea et al. [17] studied the NFBC1966 population, examining participants who had a lifetime diagnosis of psychosis. The non-participants in later follow-ups were more often patients with schizophrenia and had more psychiatric hospitalizations with more positive symptoms.

NFBC1966 consists of individuals with schizophrenia at many different stages of the disease. If we would simply study how many of these individuals could be included in clinical antipsychotic trials, this could be seen as a limitation. However, as we have been studying the representativeness of the antipsychotic trials' population compared to the population-based sample, this makes a notable advantage in the NFBC1966 population. In this type of naturalistically set up sample, we can see how many different comorbidities and other factors that may affect the treatment of schizophrenia there are in a real-life clinical population.

Another notable strength in our sample is the almost exceptionally long follow-up with the individuals with schizophrenia. As mentioned before, according to Leucht

et al. [6] in the meta-analysis of 65 antipsychotic RCTs, the median duration of follow-up was 26 weeks and there were only a few 3-year follow-ups. In this study, we used data from the 34-year follow-up, which was collected during the years 1999 to 2001, and the 43-year follow-up, which was collected during the years 2008 to 2010.

CONCLUSION

Participants in clinical trials seem to have higher PANSS scores, which seems to be the greatest simple factor difference between the populations. It is also notable that the combined exclusion criteria excludes 42.1 per cent of the population in our sample. When both the PANSS score and combined exclusion criteria were accounted for, depending on the strictness of PANSS criteria, 10.5 to 24.6 per cent of the population in the NFBC1966 34-year follow-up could be included in clinical antipsychotic trials. It seems that the NFBC1966 population is both less severely ill in the order of PANSS and also has more other factors that may affect the treatment of schizophrenia with antipsychotics. However, in the analyses done, there is no statistically significant difference between the included and excluded groups in this data.

The hypothesis for this study was that individuals in NFBC1966 are more severely ill and have more comorbidities than the individuals in clinical antipsychotic trials. This proved to be half true. Around one-third of the individuals could be excluded by factors not directly depending on schizophrenia. However, PANSS was the most common simple factor why the individuals would not be included in clinical antipsychotic trials. This may partly be because of the setup of NFBC1966. There is not any guarantee that the individuals in NFBC1966 happen to have an acute exacerbation during the follow-up, as often mentioned as an inclusion criterion. This might lead to lower scores in PANSS with the individuals of NFBC1966. However, it is also notable that the individuals excluded via combined exclusion criteria had statistically significantly more hospital treatment days than the individuals included. This might suggest that even though individuals in NFBC1966 had lower PANSS scores, the comorbidities made the management of schizophrenia more difficult in the excluded population and individuals more severely ill in other ways than simply viewed through the PANSS score.

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References

1. Niemi M, Palanteri S. Psykiatrian erikoisalan laitoshoido 2004. Sosiaali- ja terveystieteiden tutkimus- ja kehittämiskeskus, Suomen virallinen tilasto, Terveystieteiden tutkimuskeskus, Tilastotiedote 29/2005.
2. Suomalaisen Lääkäriseura Duodecimin ja Suomen Psykiatriyhdistys ry:n asettama työryhmä. Skitsofrenia. Käypä hoito -suositus. Helsinki: Suomalainen lääkäri-seura Duodecim 2020. (Cited 12.4.2021).
3. Jääskeläinen E, Isohanni M, Seppälä J, Seppälä A, Miettunen J, Koponen H. Hoitoresistentin skitsofrenian hoitomahdollisuudet. Lääketieteellinen Aikakauskirja Duodecim. 2018; 134(7):687-95.
4. Leucht S, Heres S, Kissling W, Davis JM. Evidence-based pharmacotherapy of schizophrenia. Int J Neuropsychopharmacol. 2011; 14:269-84.
5. Taipale H, Mittendor-Rutz E, Alexanderson K, Majak M, Mehtälä J, Hoti F, Jedenius E, Enkusson D, Leval A, Sermon J, Tanskanen A, Tiihonen J. Antipsychotic and mortality in a nationwide cohort of 29,823 patients with schizophrenia. Schizophrenia Research. 2018; 197:274-80.
6. Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Salanti G, Davis JM. Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. Lancet 2012; 379(9831): 2063-71.
7. Kennedy-Martin T, Curtis S, Faries D, Robinson S, Johnston J. A literature review on the representativeness of randomized controlled trial samples and implications for the external validity of trial results. Trials 2015; 16:495.
8. Gartlehner G, Hansen RA, Nissman D, Lohr KN, Carey TS. Criteria for Distinguishing Effectiveness From Efficacy Trials in Systematic Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US). 2006 Apr. Report No.: 06-0046.
9. Jääskeläinen E, Haapea M, Rautio N, Juola P, Penttilä M, Nordström T, Rissanen I, Husa A, Keskinen E, Marttila R, Filatova S, Paaso TM, Koivukangas J, Moilanen K, Isohanni M, Miettunen J. Twenty years of schizophrenia research in the Northern Finland Birth Cohort 1966: a systematic review. Schizophr Res Treatment. 2015; 2015:524875.
10. Moilanen J. The use of antipsychotic medication and its association with outcomes and brain morphometry in schizophrenia: the Northern Finland Birth Cohort 1966 Study. Doctoral Thesis. 2016 Oulun yliopisto. Acta Universitatis Ouluensis. D, Medica.
11. University of Oulu: Northern Finland Birth Cohort 1966. University of Oulu. <http://urn.fi/urn:nbn:fi:att:bc1e5408-980e-4a62-b899-43bec3755243>
12. Nordström T, Miettunen J, Auvinen J, Ala-Mursula L, Keinänen-Kiukaanniemi S, Veijola J, Järvelin M-R, Sebert S, Männikkö M. Cohort Profile: 46 years of follow-up of the Northern Finland Birth Cohort 1966 (NFBC1966). Int J Epidemiol 2021; 1-12.
13. Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, Samara M, Barbui C, Engel RR, Geddes JR, Kissling W, Stapf MP, Lässig B, Salanti G, Davis JM. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet 2013; 382(9896):951-62.
14. Leucht S, Leucht C, Huhn M, Chaimani A, Mavridis D, Helfer B, Samara M, Rabaioli M, Bächer S, Cipriani A, Geddes JR, Salanti G, Davis JM. Sixty years of placebo-controlled antipsychotic drug trials in acute schizophrenia: systematic review, bayesian meta-analysis, and meta-regression of efficacy predictors. Am J Psychiatry 2017; 174(10):927-42.

15. Taipale H, Schneider-Thoma J, Pinzón-Espinosa J, Radua J, Efthimiou O, Vinkers CH, Mittendorfer-Rutz E, Cardoner N, Pintor L, Tanskanen A, Tomlinson A, Fusar-Poli P, Cipriani A, Vieta E, Leucht S, Tiihonen J, Luykx JJ. Representation and Outcomes of Individuals With Schizophrenia Seen in Everyday Practice Who Are Ineligible for Randomized Clinical Trials. *JAMA Psychiatry* 2022; 79(3):210-218.
16. Lauronen E, Miettunen J, Vejjola J, Karhu M, Jones PB, Isohanni M. Outcome and its predictors in schizophrenia within the Northern Finland 1966 Birth Cohort. *Eur Psychiatry*. 2007 Mar;22(2):129-36.
17. Haapea M, Miettunen J, Vejjola J, Lauronen E, Tanskanen P & Isohanni M. Non-participation may bias the results of a psychiatric survey: an analysis from the survey including magnetic resonance imaging within the Northern Finland 1966 Birth Cohort. *Soc Psychiatry Psychiatr Epidemiol* 2007; 42(5):403-9.



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VIRTUAL REALITY INTERVENTION FOR PSYCHOTIC DISORDERS USING 360-DEGREE VIDEO TECHNOLOGY – DEVELOPMENT AND INITIAL PILOT FOR FEASIBILITY

ABSTRACT

Virtual reality technologies have been utilized in the treatment of psychiatric disorders by offering means to practice challenging situations in a safe environment. In this narrative description, we illustrate the development of a virtual reality-based intervention rationale to treat paranoid ideations of individuals with psychotic disorders with immersive 360-degree video material. Using 360-videos with a head-mounted display was judged as an interesting and flexible low-tech solution compared to other solutions. 360-degree videos were filmed with a head-mounted camera, simulating everyday social situations which people with paranoid delusions often find threatening. These situations were chosen by a team consisting of clinicians and an expert by experience and included commuting, grocery shopping as well as walking in a crowded street or a dark alley. Five weekly sessions with a clinician were included in the treatment protocol, following a treatment manual and individualized case formulation. The patients were exposed to the simulations using a virtual reality headset. The goals of the pilot were to evaluate the feasibility of 360-degree videos as an immersive technology and the rationale for using this technology in an exposure-based psychotherapeutic treatment, as well as to create a detailed description of the development and materials for treatment for others to follow and use. The intervention was found feasible by the clinicians and was positively received by the first pilot patients. The only observed disadvantage was nausea and dizziness caused by specific video clips. 360-degree videos were deemed suitable as a material for exposure. As far as we know, 360-degree video technology has not been previously evaluated in the context of psychotic disorders. The utility of this technology and the content created in the treatment of paranoid ideation appears promising. Based on this pilot, creating a virtual reality intervention based on exposure for psychotic disorders is possible without excessive resources and without any specific technical know-how with 360-degree videos. Developing novel forms of treatment using low technology solutions, which are easy to pilot in a day-to-day clinical environment, may bridge the gap between controlled studies and standard practice. The process of development and implementation is carefully laid out so this paper can be used as a guide for the development of similar protocols.

KEYWORDS: SCHIZOPHRENIA, PSYCHOTIC DISORDERS, PSYCHOTHERAPY, EXPOSURE, VIRTUAL REALITY

BACKGROUND

Digital health technologies are an economically viable way to assess, monitor and treat psychiatric disorders and improve access to care [1,2,3]. One of the most promising and versatile forms of technology is virtual reality (VR), and its role in psychiatry is constantly increasing [4,5]. VR as a treatment paradigm is being studied and implemented in numerous psychiatric disorders, including anxiety disorders [6,7], specific phobias [8], post-traumatic stress disorder [9] and depression [10]. VR-based treatments have also been used to improve emotion recognition skills [11], social information processing [12] and aggression management [13]. Exposure to stressful situations in a VR environment aims to improve various skills, to decrease distress related to the corresponding real-life situations and to lower the threshold of going to these situations in vivo. Bridging VR environments and real life, and transferring what has been practiced in the clinical setting with the help of a trained clinician to one's own routines, is a central goal of any VR treatment [14].

VR-based interventions have also been utilized in the assessment and treatment of psychotic disorders, including cognitive symptoms (e.g., deficits in learning, attention and executive functions) [15], hallucinations [16,17] and delusional thinking [18,19]. Simulated environments can be used to reduce paranoid symptoms and negative affect in daily life, alleviate distress caused by paranoid ideation and persecutory delusions and to reduce paranoid conviction [20,21]. In some cases, VR-assisted therapy has been associated with somewhat better treatment results compared to conventional CBT when treating psychotic disorders [22,23,24], and automated versions of VR-based psychological therapy are being developed and studied for patients with persecutory delusions [25]. As individuals with psychotic disorders often experience difficulties in verbalizing internal experiences [26], conventional psychotherapy might not be the optimal and most motivating treatment approach for many, due to its focus on verbal communication and naming or describing emotions and internal states. VR solutions may shift treatment towards a more functional approach and help to increase level of motivation for the treatment of patients with such deficits [27].

VR simulations can be created with software development or by filming 360-degree video footage. Previously, it has been reported that 360-videos might be an affordable and easy way to implement an alternative to programmed VR environments when treating social anxiety, and that

360-videos also include the sense of presence that might trigger anxiety [28]. Furthermore, study protocols to use 360-videos to treat social anxiety have been developed and some initial results of their positive impact in treating social anxiety have been reported [29,30]. However, we are not aware of earlier use of 360-videos in treating psychotic disorders.

In this paper, we present a VR pilot project of the development of suitable 360-videos and utilizing them as material for exposure with individuals suffering from a psychotic disorder and paranoid ideation. Paranoid ideation is common in individuals with a psychotic disorder and often remains in the form of anxiety and various safety behaviours even with successful medication [31]. Possible therapeutic effects of VR simulations in treating paranoid ideation include changes in theory of mind and social cognition, as deficits in them may lead to misunderstandings and misinterpretations in social situations [32,33,34]. Furthermore, it has been proposed that VR-assisted therapy may become a preferred psychological treatment for delusions and social anxiety in this patient cohort [35]. The aim is to present novel tools and technical considerations, which minimize the amount of funds, to augment previous understanding required to successfully build a VR intervention. We focus on the feasibility of 360-videos as a technical solution and the rationale of utilizing them in the context of exposure-based therapy. Patient experiences are discussed briefly and on a general level and clinician experiences in more detail.

METHODS

The potential of different VR applications in the treatment of psychotic disorders were recognized by the Division of Psychoses and Forensic Psychiatry in Helsinki University Hospital (HUS). A multidisciplinary team was formed to further analyse the current literature and to organize a project with a goal to develop and implement a VR-based treatment for patients with psychotic symptoms and social phobia. The team consisted of professionals from the fields of psychiatry, clinical psychology, psychotherapy, clinical research, and included an expert by experience to broaden the viewpoints of the team from the patients' perspective. The project focused on examining the suitability of the developed treatment as well as VR in general as a new paradigm for treating patients with psychotic disorders in Finland. In addition, different hardware and software options for routine practice were mapped. The project was performed in collaboration with HUS and the Finnish

Institute for Health and Welfare (THL). In the early phases of the project, the team also received technical consultation from Aalto University (Department of Neuroscience and Biomedical Engineering). It was decided that the pilot project would be done as a part of standard clinical practice as an experimental treatment. Physicians in charge of the treatment of patients participating in the treatment were part of the research team and the ethical considerations of the study were guided by ethical recommendations of standard clinical practice, since no patient data was included in the study.

The first phase of the project was to specify the kind of VR application that would be developed and implemented in clinical practice. Based on literature, it was laid out that VR technology could be utilized in the treatment of all core symptoms of psychotic disorders: hallucinations, delusions and cognitive deficits. Advances in AVATAR therapy, an intervention utilizing a combination of digital image and speech modulation software to create an avatar through which the therapist communicates with the patient to make voices more manageable, sparked the initial interest in these applications [36]. It was later decided that the first pilot project would focus on alleviating distress caused by paranoid ideation using VR. This decision was made considering multiple viewpoints. First, AVATAR therapy is a treatment which was originally designed to be administered with standard computers. Although AVATAR therapy has been carried out in a VR environment with a head-mounted display since the original publication [37], the team decided to proceed with a solution that was specifically a VR solution. Second, licensing the AVATAR therapy software was deemed too expensive and impractical for pilot use. Third, based on our initial review of different software options, it was recognized that focusing on treating paranoid ideation as an area of application would include the most easily available options for technical implementation. Finally, distress caused by paranoid ideation and its connection to social avoidance are common problems in both inpatient and outpatient settings, and therefore, focusing on this symptom category was seen as potentially extremely beneficial. VR presented an easily modifiable method, which could be used to encompass a variety of everyday environments that typically are associated with varying degrees of stress with respect to the patient population.

After deciding that the treatment developed during the pilot project would focus on paranoid ideation, the team shifted its attention to find the most appropriate hardware and software for implementation. From available hardware

options, the 'Meta Quest 2' (MQ2) solution was deemed the most suitable for its capability to view virtual reality content without an external computer. The MQ2 included both the head-mounted display and two controllers. The headset uses Oculus Insight technology for head and hand tracking, is equipped with a Fast-switch LCD display with a resolution of 1832 x 1920 pixels per eye and a refresh rate of 72Hz as well as 64GB of internal storage (256GB version is available as well).

Many ready-made software options and easy-to-use frameworks for the development of own software were considered, but the team ended up selecting 360-videos as the stimuli for the exposures. The team judged 360-videos as a flexible and interesting option that allows fast content creation that could be specifically tailored for an individual patient. A plan to film 360-videos and use them as material for exposure in the pilot project was laid out.

For filming the videos, an accessible and affordable hardware option was the GoPro MAX camera (GPM). The GPM is a 17 megapixel VR/Action camera with 1/2.3" (6.17 x 4.55 mm) sensor size which shoots footage in H.264 and H.265 formats. The team aspired to shoot footage in which the viewer would experience an environment from a first-person perspective with a 360-degree view. To do this, the camera was positioned in a way that there were no obstacles in front of the camera and the viewer would see as little as possible of the person filming the footage. The only position where this was possible was on top of the head of the person filming the footage. GPM is commonly used by alpine skiers and mountain bikers, and the standard package includes a helmet mount for the camera. However, filming the footage with a helmet-mounted camera in public places may result in an abnormal amount of people looking at the camera and therefore would not represent a real-life situation. Despite this potential problem, it was decided to film the footage with the GPM attached to a helmet.

For the stimuli, footage from common daily life situations, which commonly provoke delusional thinking and anxiety and which people with psychotic disorders tend to avoid, were filmed. The situations selected were visiting a grocery store, walking in a dark alley, travelling via public transport and walking through crowded spaces (e.g., shopping malls). Four videos were shot spanning these situations. Each video was 20-40 minutes in length and was divided into 3-4 shorter parts. The videos were stored in the internal storage of the headset. The option to host the videos on YouTube was considered since the MQ2 has a native YouTube application, but the large file sizes of the

360-degree videos made this solution impractical.

The treatment manual created during the project was modelled after the protocol used in the study by Pot-Kolder and colleagues in 2018 [20] with a smaller number of sessions. The treatment in the pilot consisted of five weekly sessions with a clinical psychologist with experience in psychological interventions. Every session was 60 minutes in length. The first session was dedicated to the client getting acquainted with the clinician and the treatment protocol as well as for working out an individualized case formulation, and the last session for reflecting on the experiences during the treatment. The three sessions in the middle were structured: 10 minutes on getting started and reflecting on the last session, 40 minutes of exposure exercises within the VR environment and 10 minutes of reflection. Patients and the clinicians communicated during the exposure to explore the experiences of the patient in each setting and to recognize and drop safety behaviours and to question harm expectancies. It was made clear from the beginning that the focus of the pilot treatment was to trial the feasibility of the treatment protocol, and this was discussed with all the participants. Furthermore, it was explicitly stated that the clinician and the patient were allowed to examine and try out the hardware and software in a cooperative and collaborative manner to make the procedure more flexible.

Standardized questionnaires were used both at the beginning and after treatment to evaluate the intervention and to scout out initial changes that might arise during the intervention. Further, feedback from the patient was gathered after every session. However, in this paper we focus on the clinicians' experiences, whereas the patients' experiences will be addressed at a general level and in detail in a separate study. Clinicians' viewpoints were gathered with predetermined questions ("How would you describe the overall clinical value of VR treatments when treating paranoid thoughts?", "How does utilizing VR affect the therapeutic alliance with the patient or to the effectiveness of psychosocial treatment with patients with a psychotic disorder?", "How would you generally describe patients who would benefit from VR treatments that you have now implemented?", "How could the treatment protocol now implemented be further developed?", "How easy or hard would you describe implementing a new VR-based treatment protocol into clinical practice?").

The patients were recruited from both inpatient and outpatient clinics in HUS as a part of routine clinical practice. Information about the pilot treatment was given to multidisciplinary teams in their workplace to scout out

potential patients. The clinics were searching for patients who suffered from thoughts and emotions that hindered their ability to visit social environments and therefore deal with everyday situations. The only exclusion criterion for patient participation was an epilepsy diagnosis. Other strict inclusion and exclusion criteria were not laid out since the team wanted to test the intervention with patients with different history and status. Suitable patients were offered voluntary participation in the pilot as part of their treatment. Before starting the exercises, the patients were informed that some people may experience nausea and motion sickness while using the headset and that the exercise could be terminated at any point if the patient so chose.

RESULTS

We provide experiences of the first three patients receiving the treatment and present results from three different perspectives. First, the clinicians' experiences with the developed 360-videos and the treatment protocol are presented in detail. Second, the patient experiences will be presented at a general level. Finally, results regarding the suitability of the selected technology and the pilot process are presented.

Clinicians working with the patients (authors LS and HK) evaluated that the developed intervention and the materials used offered a more direct and accurate perspective on the thought processes of individuals and an easy-to-use way to administer an intervention based on exposure. The main clinical benefit of the intervention was that patients receiving the treatment were encouraged to face stressful real-life situations and to start in vivo exposure. Using the headset together with the patient created an environment of cooperation and common problem sharing which often led to a humorous and relaxed atmosphere. However, setting up the system prior to the exposure took time even when the patient and the clinician became experienced with the system, which must be considered when planning the schedule. Allocating more than 60 minutes per session seems therefore more optimal. The treatment rationale and manual were deemed by the clinicians as structured and comprehensive enough to offer a safe frame for therapeutic alliance and exposure exercises, and to enable any clinical professional experienced in psychological treatments for psychotic disorders to implement the intervention. Limiting the intervention length to five sessions was deemed suitable for the pilot phase. Because of its length, the treatment

protocol was easy to implement since both the clinician and the patient could easily commit to the treatment. The detailed responses of the clinicians regarding the feasibility of the piloted protocol and VR treatments can be viewed from *Table 1*.

From the clinicians' perspective, the patients were interested and excited about the treatment they received. After every session, patients gave excellent reviews regarding the working methods of the session. The most common negative side effect while conducting the treatment was nausea and dizziness caused by the video footage. This was

Table 1. Employment status of users who filled in FTN

Question	Clinicians' response
How would you describe the overall clinical value of VR treatments when treating paranoid thoughts?	The overall clinical value of VR treatment when treating paranoid thoughts seems to be prominent because it offers the possibility to perceive the ideation as it arises in concrete situations. VR treatment offers a functional approach to treating paranoid thoughts. The patients find it easier to recognize and share their experiences in VR exposure compared to generally used self-observations.
In your opinion, how does utilizing VR affect the therapeutic alliance with the patient or to the effectiveness of psychosocial treatment with patients with a psychotic disorder?	The manual of the treatment was structured enough to offer a safe frame and space for the therapeutic alliance. The VR system with all the technical operations provides the alliance with cooperation and common problem sharing that give space to relaxed and humorous atmosphere. This kind of parasympathetic activation is essential to start and benefit from the exposure.
How would you generally describe patients who would benefit from VR treatments that you have now implemented?	The patients with increased avoidance and a long-term isolation would be the main target group for the treatment. VR treatment can work for them as a first step to explore social situations and the world outside. After VR exposure the patients may have more interest and courage to proceed towards real-life situations. Also, patients with many social fears and distorted interpretations could benefit from exploring VR situations with clinician, to process perceptions, emotions and thoughts.
How could the treatment protocol now implemented be further developed?	The treatment itself is well structured and flexible enough to form individual targets for each patient. The length of one session is 60 minutes. It might be better to have longer sessions (e.g., 75 minutes) to make sure that the absolute duration of exposure is long enough. The 360-video materials could be further developed. The main problem with them is the nausea and dizziness caused by the movement and rotation of the camera. There are only four different videos that are all taken in wintertime and in the public spaces with only few individual contacts. A wider variation of situations could make exposures more individually planned and effective.
How easy or hard would you describe implementing a new VR-based treatment protocol into clinical practice?	Implementing a new VR-based treatment protocol requires trained clinicians and overall information of the treatment to help find suitable patients for the treatment. The written manual of the treatment is comprehensive enough to enable any clinical psychologist experienced in psychosis to implement the treatment. A decent induction and a possibility for supervision are needed. To make sure of a successful implementation there should also be an adequate amount of hardware and working spaces large enough for VR system.

related to specific videos created for the pilot, which included a lot of head rotations by the person filming the material. Any other adverse effects of the treatment weren't detected. Despite these challenges, going into the virtual world was generally perceived as a fun and an inspiring "new thing" by the patients.

The suitability of the 360-degree video technology was evaluated throughout the project. Creating the intervention using 360-degree videos as material for simulations allowed the project to be implemented without excessive time or monetary resources or prior technical know-how. The materials and technology were immersive enough to activate similar reactions and thought processes from the patients compared to corresponding real-life settings as evaluated by two individual clinicians. Developing the video materials further can be seen as an equally viable option as simulations created with software development. The pilot itself proved valuable for the patients it was tried on and the intervention is seen as the first concrete step on creating VR-based treatment protocols for standard practice.

DISCUSSION

This study presented a VR-based treatment protocol for paranoia and delusional thinking and initial findings from a clinical pilot project. Our results indicate that it is feasible to create a VR-based exposure intervention using 360-degree video technology and that utilizing this intervention can be highly beneficial for individuals with a psychotic disorder. Our findings can be used to create a road map for further development and research as well as a guide for similar pilot ventures.

Exposure exercises within a VR environment can be seen as a method for addressing safety behaviours, cognitive biases and emotions supporting the assumptions behind them as well as for improving patients' courage, confidence and skills to face stressful real-life situations. By confronting stressful situations in a safe and controlled environment, it may be possible to question false and harmful beliefs more easily. A VR-based intervention may also facilitate the understanding of the patients' internal experiences for the clinician, as both participants are immersed in the same environment. This method may move the therapeutic situation into "here and now", which might facilitate change in therapy and partially explain the results of the superiority of VR-based interventions compared to traditional therapeutic interventions when treating psychotic disorders.

Besides creating immersive exposure experiences, using VR can foster therapeutic working alliance by offering shared problems the patient and clinician can tackle together. Our initial results of the clinicians' experiences suggest that this kind of relaxed environment can work as a path for parasympathetic activation, which may be essential to start and benefit from exposure [38]. Of course, VR environments can also be used to relax and reflect after the exercise. In further research endeavours, the activation of the nervous system before, during and after the exposure could be measured with physiological measures and sensors. Our preliminary findings suggest that VR-based interventions are also seen as a novel and interesting treatment option from the patients' perspective, which might have a positive effect on overall treatment motivation.

Despite the numerous potential benefits and possibilities of VR-based interventions, some negative features of VR have also been reported. The most frequently reported negative effect of VR treatment is "cyber sickness", which refers to a feeling of motion sickness during VR simulations [39]. These perceived disadvantages need to be taken into consideration from an ethical perspective when designing treatment protocols that incorporate VR simulations. This was also apparent in our clinical pilot. This can be controlled by avoiding filming material in which the camera moves, which in our material was caused by the head movement of the person who filmed the footage. There is a possibility that an intervention based on VR exposure includes risks for psychological harm when conducted by an inexperienced clinician. Therefore, it is required that only clinicians trained in psychotherapeutic methods and at least basic principles in exposure carry out the treatment, and that the material used in exposure is selected in a trauma-sensitive manner with the individual case formulation in mind. Further, sensors that monitor the physiological response of the patient during exposure could be used to track the suitability of the selected materials with patients with difficulty articulating their experiences verbally.

Compared to computer-generated VR simulations, 360-degree videos are an interesting alternative for providing immersive experiences as a part of exposure exercises. Filming the videos is not overly complicated with a head-mounted camera. It was hypothesized beforehand that attaching the camera to a helmet would attract an unnecessary number of glances from the bystanders, but this was not the case. With all the videos, the material filmed showed situations which looked and felt normal. Benefits of using 360-degree videos are that they may represent lifelike situations in more detail

compared to programmed environments and therefore might lead to deeper levels of immersion, and that exposure training can be done in various environments, including the patient's home [29]. As 360-degree videos can be very large files, we recommend that such videos be filmed with a level of quality which allows multiple videos to be stored in the internal memory of a VR headset or which could be uploaded to a video streaming service (e.g., YouTube) relatively quickly. As with the video quality, a balance needs to be struck with the length of the videos. Longer videos could lower the time which is used in selecting the video, but shorter videos would allow a specific situation to be experienced more easily without the need to manually rewind the video.

A wide library of 360-videos would allow a tailored exposure therapy based on the individual needs of the patient. One solution to speeding up the process of using 360-videos as clinical tool with psychotic disorders would be a shared video library available for multiple researchers and clinical units. Such practice is already taking off in Finland. As the filming process of 360-degree videos isn't either difficult nor time-consuming, there is a possibility to create tailor-made materials for each patient. One need for tailored material has stemmed from a specific clinical problem in an inpatient unit in HUS where treatment time in a ward is lengthened because the patients' fears are in some way related to their own home. Creating 360-degree video materials from the individuals' home, with consent, could allow the patient to practice dealing with thoughts and emotions which the environment activates. Overall, VR-based interventions can make exposure as a therapeutic method more accessible to all in need, including those who cannot visit stressful environments in real life and those whose anxiety reaches levels which prevent in vivo exposure exercises.

CONCLUSIONS

To our knowledge, 360-degree video technology as a basis for exposure hasn't been used in the context of treating individuals with psychotic disorders. Based on our findings, this technology passes the initial tests of feasibility and calls for further investigation. The presented results show promise in widening the treatment options of psychotic disorders as the materials and treatment rationale received positive feedback from both patients and clinicians. However, findings are only indicative and can be used to form hypotheses for further research with carefully designed experimental studies and representative samples.

In the Helsinki University Hospital, further studies will be conducted in the following years to fully realize the potential of VR treatments as an integrated part of other treatment. We hope that our work will be a source of inspiration for other research endeavours and lower the threshold for using VR treatments with this patient cohort.

LIST OF ABBREVIATIONS

VR (virtual reality), HUS (Helsinki University Hospital), THL (Finnish Institute for Health and Welfare), MQ2 (Meta Quest 2 VR headset), GPM (GoPro Max camera).

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Patient records or data were not used in the study as the study is focused on the development and first clinician experiences of a new virtual reality intervention with a novel technical paradigm. Physicians in charge of the treatment of patients included in the study were part of the research team and the ethical considerations of the study was guided by ethical recommendations of standard clinical practice. Taking part in the treatment was voluntary for the patients and the decision to offer the intervention to a patient was decided with the physician in charge of the patient's treatment and the team of medical professionals who conducted the treatment. The need for informed consent and ethical approval was waived by guidance of the Research Ethics Committee of Helsinki University Hospital (HUS) as the study does not meet the criteria for medical research. The national legislation in Finland (Law on medical research 1999/488) states that such actions are not necessary if the criterion for medical research is not met. We confirm that the study was performed in accordance with relevant guidelines and regulations of the Declaration of Helsinki.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analysed during this study are included in this published article and its supplementary information files.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

KM oversaw the design and implementation of the project and writing of the manuscript. He also filmed the 360-video materials and instructed the clinicians. LS was one of the two clinicians performing the intervention, she also was a part of designing the treatment protocol and was a contributor in writing the manuscript. ML participated in the design of the project and was a major contributor in

writing the manuscript. HK was one of the two clinicians performing the intervention, she also was a part of designing the treatment protocol and was a contributor in writing the manuscript. BK acted as the physician in charge of the treatment protocol, participated in the design of the project and was a major contributor in writing the manuscript. MM participated in the design of the project and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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References

1. Mikkonen K, Wegelius A, Salmijärvi L, Paunio T, Kiesepä T. Digital health technologies in the psychosocial treatment of core symptoms of psychotic disorders-literature review and practical aspects. *Psychiatria Fennica*. 2020.
2. Rus-Calafell M, Schneider S. Are we there yet?!—a literature review of recent digital technology advances for the treatment of early psychosis. *Mhealth*. 2020;6.
3. Pot-Kolder R, Veling W, Geraets C, Lokkerbol J, Smit F, Jongeneel A, Ising H, Van Der Gaag M. Cost-effectiveness of virtual reality cognitive behavioral therapy for psychosis: health-economic evaluation within a randomized controlled trial. *Journal of medical Internet research*. 2020 May 5;22(5):e17098.
4. Cieślik B, Mazurek J, Rutkowski S, Kiper P, Turolla A, Szczepańska-Gieracha J. Virtual reality in psychiatric disorders: A systematic review of reviews. *Complementary Therapies in Medicine*. 2020 Aug 1;52:102480.
5. Emmelkamp PM, Meyerbröker K. Virtual reality therapy in mental health. *Annual review of clinical psychology*. 2021 May 7;17:495-519.
6. Oprış D, Pinteş S, García Palacios A, Botella C, Szamosközi Ş, David D. Virtual reality exposure therapy in anxiety disorders: a quantitative meta analysis. *Depression and anxiety*. 2012 Feb;29(2):85-93.
7. Parsons TD, Rizzo AA. Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *Journal of behavior therapy and experimental psychiatry*. 2008 Sep 1;39(3):250-61.
8. Czerniak E, Caspi A, Litvin M, Amiaz R, Bahat Y, Baransi H, Sharon H, Noy S, Plotnik M. A novel treatment of fear of flying using a large virtual reality system. *Aerospace medicine and human performance*. 2016 Apr 1;87(4):411-6.
9. Cuperus AA, Laken M, van den Hout MA, Engelhard IM. Degrading emotional memories induced by a virtual reality paradigm. *Journal of Behavior Therapy and Experimental Psychiatry*. 2016 Sep 1;52:45-50.
10. Ioannou A, Papastavrou E, Avraamides MN, Charalambous A. Virtual reality and symptoms management of anxiety, depression, fatigue, and pain: a systematic review. *SAGE open nursing*. 2020 Aug;6:2377960820936163.
11. Seinfeld S, Arroyo-Palacios J, Iruretagoyena G, Hortensius R, Zapata LE, Borland D, de Gelder B, Slater M, Sanchez-Vives MV. Offenders become the victim in virtual reality: impact of changing perspective in domestic violence. *Scientific reports*. 2018 Feb 9;8(1):2692.
12. Verhoef RE, van Dijk A, Verhulp EE, de Castro BO. Interactive virtual reality assessment of aggressive social information processing in boys with behaviour problems: A pilot study. *Clinical psychology & psychotherapy*. 2021 May;28(3):489-99.
13. Klein Tunte S, Bogaerts S, Bulten E, Keulen-de Vos M, Vos M, Bokern H, IJzendoorn SV, Geraets CN, Veling W. Virtual reality aggression prevention therapy (VRAPT) versus waiting list control for forensic psychiatric inpatients: a multicenter randomized controlled trial. *Journal of clinical medicine*. 2020 Jul 16;9(7):2258.
14. Morina N, Ijntema H, Meyerbröker K, Emmelkamp PM. Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments. *Behaviour research and therapy*. 2015 Nov 1;74:18-24.
15. Miskowiak KW, Jespersen AE, Kessing LV, Aggestrup AS, Glenthøj LB, Nordentoft M, Ott CV, Lumbye A. Cognition Assessment in Virtual Reality: Validity and feasibility of a novel virtual reality test for real-life cognitive functions in mood disorders and psychosis spectrum disorders. *Journal of Psychiatric Research*. 2022 Jan 1;145:182-9.

16. Du Sert OP, Potvin S, Lipp O, Dellazizzo L, Laurelli M, Breton R, Lalonde P, Phraxayavong K, O'Connor K, Pelletier JF, Boukhalfi T. Virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: a pilot clinical trial. *Schizophrenia research*. 2018 Jul 1;197:176-81.
17. Dellazizzo L, Potvin S, Phraxayavong K, Dumais A. Exploring the benefits of virtual reality-assisted therapy following cognitive-behavioral therapy for auditory hallucinations in patients with treatment-resistant schizophrenia: a proof of concept. *Journal of clinical medicine*. 2020 Sep 30;9(10):3169.
18. Valmaggia LR, Day F, Rus-Calafell M. Using virtual reality to investigate psychological processes and mechanisms associated with the onset and maintenance of psychosis: a systematic review. *Social psychiatry and psychiatric epidemiology*. 2016 Jul;51:921-36.
19. Veling W, Moritz S, Van Der Gaag M. Brave new worlds—review and update on virtual reality assessment and treatment in psychosis. *Schizophrenia bulletin*. 2014 Nov 1;40(6):1194-7.
20. Pot-Kolder RM, Geraets CN, Veling W, van Beilen M, Staring AB, Gijsman HJ, Delespaul PA, van der Gaag M. Virtual-reality-based cognitive behavioural therapy versus waiting list control for paranoid ideation and social avoidance in patients with psychotic disorders: a single-blind randomised controlled trial. *The Lancet Psychiatry*. 2018 Mar 1;5(3):217-26.
21. Geraets CN, Veling W, Witlox M, Staring AB, Matthijssen SJ, Cath D. Virtual reality-based cognitive behavioural therapy for patients with generalized social anxiety disorder: a pilot study. *Behavioural and cognitive psychotherapy*. 2019 Nov;47(6):745-50.
22. Gega L, White R, Clarke T, Turner R, Fowler D. Virtual environments using video capture for social phobia with psychosis. *Cyberpsychology, Behavior, and Social Networking*. 2013 Jun 1;16(6):473-9.
23. Freeman D, Bradley J, Antley A, Bourke E, DeWeever N, Evans N, Černis E, Sheaves B, Waite F, Dunn G, Slater M. Virtual reality in the treatment of persecutory delusions: randomised controlled experimental study testing how to reduce delusional conviction. *The British Journal of Psychiatry*. 2016 Jul;209(1):62-7.
24. Dellazizzo L, Potvin S, Phraxayavong K, Dumais A. One-year randomized trial comparing virtual reality-assisted therapy to cognitive-behavioral therapy for patients with treatment-resistant schizophrenia. *npj Schizophrenia*. 2021 Feb 12;7(1):9.
25. Freeman D, Lister R, Waite F, Yu LM, Slater M, Dunn G, Clark D. Automated psychological therapy using virtual reality (VR) for patients with persecutory delusions: study protocol for a single-blind parallel-group randomised controlled trial (THRIVE). *Trials*. 2019 Dec;20:1-8.
26. Trémeau F. A review of emotion deficits in schizophrenia. *Dialogues in clinical neuroscience*. 2022 Apr 1.
27. Rus-Calafell M, Garety P, Sason E, Craig TJ, Valmaggia LR. Virtual reality in the assessment and treatment of psychosis: a systematic review of its utility, acceptability and effectiveness. *Psychological medicine*. 2018 Feb;48(3):362-91.
28. Holmberg TT, Eriksen TL, Petersen R, Frederiksen NN, Damgaard-Sørensen U, Lichtenstein MB. Social anxiety can be triggered by 360-degree videos in virtual reality: a pilot study exploring fear of shopping. *Cyberpsychology, Behavior, and Social Networking*. 2020 Jul 1;23(7):495-9.
29. Stupar-Rutenfrans S, Ketelaars LE, van Gisbergen MS. Beat the fear of public speaking: Mobile 360 video virtual reality exposure training in home environment reduces public speaking anxiety. *Cyberpsychology, Behavior, and Social Networking*. 2017 Oct 1;20(10):624-33.

30. Clemmensen L, Bouchard S, Rasmussen J, Holmberg TT, Nielsen JH, Jepsen JR, Lichtenstein MB. Study protocol: exposure in virtual reality for social anxiety disorder -a randomized controlled superiority trial comparing cognitive behavioral therapy with virtual reality based exposure to cognitive behavioral therapy with in vivo exposure. *BMC psychiatry*. 2020 Dec;20:1-9.
31. Moutoussis M, Williams J, Dayan P, Bentall RP. Persecutory delusions and the conditioned avoidance paradigm: towards an integration of the psychology and biology of paranoia. *Cognitive neuropsychiatry*. 2007 Nov 1;12(6):495-510.
32. Gainsford K, Fitzgibbon B, Fitzgerald PB, Hoy KE. Transforming treatments for schizophrenia: Virtual reality, brain stimulation and social cognition. *Psychiatry research*. 2020 Jun 1;288:112974.
33. Nijman SA, Veling W, Greaves-Lord K, Vos M, Zandee CE, Aan Het Rot M, Geraets CN, Pijnenborg GH. Dynamic interactive social cognition training in virtual reality (DiSCoVR) for people with a psychotic disorder: single-group feasibility and acceptability study. *JMIR mental health*. 2020 Aug 7;7(8):e17808.
34. Green MF, Horan WP, Lee J. Social cognition in schizophrenia. *Nature Reviews Neuroscience*. 2015 Oct;16(10):620-31.
35. Berkhof M, van der Stouwe EC, Lestestuijver B, van't Hag E, van Grunsven R, de Jager J, Kooijmans E, Zandee CE, Staring AB, Pot-Kolder RM, Vos M. Virtual reality cognitive-behavioural therapy versus cognitive-behavioural therapy for paranoid delusions: a study protocol for a single-blind multi-Centre randomised controlled superiority trial. *BMC psychiatry*. 2021 Dec;21(1):1-0.
36. Leff J, Williams G, Huckvale MA, Arbuthnot M, Leff AP. Computer-assisted therapy for medication-resistant auditory hallucinations: proof-of-concept study. *The British Journal of Psychiatry*. 2013 Jun;202(6):428-33.
37. Dellazizzo L, Potvin S, Phraxayavong K, Lalonde P, Dumais A. Avatar therapy for persistent auditory verbal hallucinations in an ultra-resistant schizophrenia patient: a case report. *Frontiers in Psychiatry*. 2018 Apr 16;9:131.
38. Souza RR, Robertson NM, Pruitt DT, Gonzales PA, Hays SA, Rennaker RL, Kilgard MP, McIntyre CK. Vagus nerve stimulation reverses the extinction impairments in a model of PTSD with prolonged and repeated trauma. *Stress*. 2019 Jul 4;22(4):509-20.
39. Rebenitsch L, Owen C. Review on cybersickness in applications and visual displays. *Virtual Reality*. 2016 Jun;20:101-25.



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ASSISTED LIVING FOR THE MENTALLY ILL – FEASIBILITY OF THE SIMPLE TAXONOMY FOR SUPPORTED ACCOMMODATION (STAX-SA) IN FINLAND PORVOO ASPA-PROJECT

ABSTRACT

Although development and growth of assisted living (AL) services for the severely mentally ill (SMI) has lasted for decades, and is still ongoing, research on AL services is scarce. Furthermore, the broad variation in AL service models, lack of global taxonomy for AL services and inconsistent reporting of AL service habitats makes the evaluation and comparison of AL services challenging. The purpose of the current study was, for the first time in Finland, to evaluate the applicability of the international Simple Taxonomy for Supported Accommodation (STAX-SA) for recategorization of current national AL service categories for the mentally ill. Data for the study is obtained from the Porvoo ASPA-project. Our main finding was that the correspondence to STAX-SA categorization was good, as 64.7% of the AL service levels could directly be classified to certain STAX-SA types. The strength of STAX-SA categorization was the ability to describe the majority of the 24-hour and part-time service units. STAX-SA ability to describe AL services weakened as the level of AL service decreased but remained reasonable. STAX-SA as a methodological tool has potential in enabling comparative studies on AL services based on the level they provide. STAX-SA has strengths in describing AL units and the services provided in them, especially by differentiating custodial care units from rehabilitation units in AL.

KEYWORDS: ASSISTED LIVING, MENTAL ILLNESS, TAXONOMY, DEHOSPITALIZATION, PORVOO ASPA-PROJECT, STAX-SA, SMI

INTRODUCTION

For decades, as part of the global deinstitutionalization process, asylums have been replaced by a complex network of community-based services for individuals suffering from severe mental illnesses (SMI) (1). Growth of specific assisted living (AL) units providing different levels of AL services for the mentally ill, and also specific AL units providing a good deal of these services, has occurred both globally as well as in Finland (2). These services constitute an essential part of the mental health rehabilitation care pathway, especially for those with complex needs. AL services strive to enable individuals with SMI to have an ordinary, inclusive and everyday life in the community by maintaining and practising their independence skills. AL services' purpose is not only to maintain but also to improve these skills for individuals with SMI, so they can manage with less support over time (2–5). Due to the deteriorating, long-lasting and often changing nature of mental illness, the need and level of supportive services may vary over time (3). Thus, AL services are also expected to cope with possible exacerbation phases of mental illness. Consequently, AL services are expected to provide appropriate types of support to respond to the needs of the SMI at different stages of their disorder's lifespan. Recent studies have acknowledged the various benefits of AL services for their habitants, such as increased satisfaction in life compared to psychiatric inpatient treatment (5–7).

Although development and growth of AL services for the SMI has lasted for decades, and is still ongoing, research on AL services is scarce (5,6). For instance, two consecutive Cochrane Reviews by Chilvers et al. 2002 and in 2006 identified no significant randomized controlled trials with adequate quality (8,9). In the past decade, research on AL services has mainly been descriptive, and the need to develop appropriate tools for research purposes in order to evaluate AL service providers and AL habitants has been emphasized. Examples of these are QuIRC-SA for quality assessment of AL services and The Simple Taxonomy for Supported Accommodation (STAX-SA) for a global categorization of AL services (10,11). In the few studies published, the research methodology and data quality have been heterogeneous, which makes it difficult to perform trustworthy synthesis of AL services (5,6). Furthermore, the broad variation in AL service models, lack of global taxonomy for AL services and inconsistent reporting of AL service habitants makes the evaluation and comparison of AL services challenging (5,6,11).

In Finland, it is known that individuals in psychiatric inpatient treatment are often also living in AL units and receiving AL services. Also, the rapid dehospitalization process might have led to the placement of individuals to AL services based on availability rather than a need for specific AL services. Therefore, it is assumable that some habitants in AL services are inappropriately placed into AL services.

To be able to reliably compare evidence-based knowledge on AL services would be of essential importance for staff working in AL units, for researchers, and for policy makers when they evaluate what kind of AL services are effective, and for whom (6,11,12). This is crucial, especially now in Finland, where transition to wellbeing services counties from a previously municipality funded social and healthcare model has occurred (13). The goal of this Finnish health and social services reform is to improve the quality and availability of services, including mental health services (14).

In Finland, current categorization of AL units into three tiers is based on the social welfare act, which also describes the AL service level provided in each tier (15). The first and most supportive tier is sheltered housing, providing 24-hour service assistance (referred hereafter as 24-hour service). The second tier is sheltered housing, providing part-time assistance (referred hereafter as part-time service). The first and second tier are somewhat institutional in nature and shared with others with similar needs. The third tier is intended for those with the least need of AL services. It is named Supported living and supported accommodation (referred hereafter as supported living). This is an arrangement in which the habitant lives either in the rented or owner occupied flat or other similar type of housing, and is not moving in the separate housing unit.

The purpose of the current study is, for the first time in Finland, to evaluate the applicability of the international Simple Taxonomy for Supported Accommodation (STAX-SA) for recategorization of current national AL service categories for the mentally ill (16). The STAX-SA, with five types defined, is based on four domains (staffing location, level of support, move-on and physical setting) and is assumed to provide deeper insight into the content of AL services compared to the current three-level categorization based on the Social Welfare act (15). The data for AL services for this study are obtained from the Porvoo ASPA-project.

AIMS

First, the AL service units are recategorized following the STAX-SA criteria and taxonomy and the results are

mirrored to the current three-level categorization of AL. Secondly, the feasibility of recategorization to STAX-SA is evaluated by the AL unit managers. Thirdly, the distribution of habitants in AL services according to gender and diagnoses are explored from the current three-level system to the STAX-SA five-level categorization. We will also present the detailed description of the protocol of the Porvoo ASPA-project.

MATERIAL AND METHODS

MATERIAL

The Porvoo ASPA-project was designed to enable a comparative longitudinal study setup to evaluate the outcomes and effectiveness of AL services in rehabilitation of the SMI in Finland.

As *Figure 1* shows, the Porvoo ASPA-project consists of four main phases: I) Planning, II) Recruitment and Collaboration, III) Data collection plan, and IV) Data analysis phase. For a detailed description of the rationale please see *Supplemental 1*. The current study will focus on the Data Analysis phase and the feasibility of the STAX-SA.

Figure 1. Porvoo ASPA-project phases and timeline part of the rationale

Planning 2/2020 – 4/2022	Back-ground	Assisted living (AL) for mentally ill—a systematic literature review and its recommendations. Ketola&Jahangiri et al. 2021 <ul style="list-style-type: none"> • There is a need for evidence-based longitudinal studies evaluating different types and costs of AL as well as quality of care and outcome for AL habitants. 	AL in relation to use of psychiatric inpatient and outpatient care - A 23-year time-trend analysis of national indicators from Finland. Jahangiri et al. 2022 <ul style="list-style-type: none"> • The decrease of psychiatric inpatient treatment and simultaneous increase in AL habitant rates has not increased outpatient care in the same ratio. • For some reason the growth within AL services has concentrated in Supported living rather than 24-hour and part-time service.
	Screening	Eligibility criteria for cities entering the study <ul style="list-style-type: none"> • Population of more than 50 000 • Minimum of 100 AL service habitants 	20 eligible cities of total of 309 cities in Finland <ul style="list-style-type: none"> • Two cities contacted
	Enrolment	City of Porvoo agreed on participation to the study Research permits were obtained from Porvoo municipality and from the Northern-Ostrobothnia Hospital District, Oulu University hospital, Psychiatry	



Porvoo ASPA project				
Recruitment and collaboration 5/2022 -7/2022	Re-cruitment	AL units (n=25) are categorized to: <ul style="list-style-type: none"> • AL with 24-hour service n=16 • AL with part-time service n=14 • Supported living n=14 	Two types of data sets identified	Individual-level data of habitants from Porvoo residing in AL units (n=348) are categorized to: <ul style="list-style-type: none"> • AL with 24-hour service • AL with part-time service • Supported living
	Collaboration	Preliminary discussion on what type of data is available and necessary for the research		
		A research seminar on 3.6.2022 <ul style="list-style-type: none"> • 16 (67%) AL units attended seminar • 23 (92%) AL units participated in the study 		Multiple meetings from 6-9/22 between authors EJ, JK and city of Porvoo employees
Methodology 7/2022 -8/2022	Questionnaires	Data 1 for AL service providers <ul style="list-style-type: none"> • Cross-sectional data • Filled by AL unit managers Research focus on: <ul style="list-style-type: none"> • Types and frequency of services provided in AL units • Habitant demographics • Use of staff and education and costs 	The need of a global taxonomy was identified <ul style="list-style-type: none"> • The Simple Taxonomy for Supported Accommodation (STAX-SA) was chosen for the study Development of data collection forms	Data 2 for AL service habitants from Porvoo <ul style="list-style-type: none"> • Three-year (2020-2022) register-based data • Collected from electronic patient registers by city of Porvoo employees Research focus on: <ul style="list-style-type: none"> • Sociodemographic and clinical characteristics • Reason for AL and outcome of AL • Mortality in AL
Data collection 8/2022 - 4/2023 and analysis				
Data analysis 4/2023-onwards	Validation	STAX-SA feasibility from Data 1 Purpose of this study		
	Reporting	Several articles planned to be submitted to international, peer-reviewed scientific journals from Data 1 and 2		

CURRENT CATEGORIZATION OF AL UNITS IN FINLAND

In Finland social services and health services are governed by the Social Welfare act and the Health Care act (15,17). The purpose of the acts is to secure the basic needs for individuals in their daily life and promote equality in society, as well as promoting health, welfare, function and social inclusion of the people. By law, the wellbeing services counties are obligated to secure social services, such as financial aid, food and cleaning support, clothing, social rehabilitation and housing, as well as healthcare services such as specialized and basic healthcare for all its inhabitants in an equal way. The wellbeing service counties can either provide AL services themselves or organize them by buying AL services from private businesses and/or non-profit organizations.

The current Social Welfare act categorizes AL services provided in AL units or AL services to habitants as follows:

Supported living and supported accommodation.

The habitant lives in his/her own apartment and the services such as social rehabilitation and financial support are provided to the person on a regular basis. The habitants must be able to take care of their basic daily needs such as hygiene. The staff is not in the immediate proximity of the unit. This type of AL service causes the least cost in Finland, both for the habitant and for society (15).

Sheltered housing with part-time service.

The habitant lives in an AL unit owned and governed by the AL service provider. The staff is available for the habitant on-site and on a daily basis, but not during night-time. In this type of living the AL service provider must produce the necessary food, cleaning, clothing, health and social services that the habitant's needs require. The staff is in the same AL unit as the habitant (15).

Sheltered housing with 24-hour service.

The habitant lives in an AL unit owned and governed by the AL service provider. The staff is available for the habitant 24/7. In this type of living the AL service provider has to produce the necessary food, cleaning, clothing, health and social services that the habitant's needs require (15). The staff is in the same AL unit as the habitant, and the staff is available 24/7 which makes it the most expensive type of AL service in Finland for the habitant and society.

THE SIMPLE TAXONOMY FOR SUPPORTED ACCOMMODATION

McPherson et al. 2018 developed a compact categorical taxonomy of AL services aiming to identify the key elements from different AL services: The Simple Taxonomy for Supported Accommodation (STAX-SA) (11). The taxonomy comprises five AL types according to the AL service level, presented in [Table 1](#). These AL service levels are based on the key characteristics of four domains covering: staffing location, level of support, emphasis on move-on and physical setting.

Table 1. The Simple Taxonomy for Supported Accommodation (STAX-SA) AL service levels and domains (11)

	AL service level				
Domain	Type 1	Type 2	Type 3	Type 4	Type 5
Staffing location	Staff on-site	Staff on-site	Staff on-site	No staff on-site	Staff on-site
Level of support	High support	High support	Moderate support	Low/moderate support	No support
Move-on	Limited emphasis on move-on	Strong emphasis on move-on	Strong emphasis on move-on	Limited emphasis on move-on	Limited emphasis on move-on
Physical setting	Congregate setting	Congregate setting	Congregate setting	Individual Accommodation	Congregate setting

METHODS

For the purposes of the current study, at the first stage, AL service units' provider-level data was collected from AL service managers from June to December 2022 using the structured questionnaire developed for this study (*Supplemental Table 1*). Each AL service manager answered the questionnaire in terms of each AL service level the unit provided to their inhabitants. Thus, the range of AL service levels per unit could vary from 1 to 3. The managers were asked to report aggregated data on inhabitants by their psychiatric diagnostic category using the following diagnostic hierarchy, starting from most severe: schizophrenia, other psychotic, affective and other disorders, as well as substance abuse.

At the second stage, the current three AL service levels, according to social welfare act, of the AL units were recategorized into five types, utilizing provider-level data following the criteria of STAX-SA, by authors EJ and TK (11). The four domains of the STAX-SA and their scoring are presented in *Table 2*. If the AL service level did not fit into STAX-SA unambiguously, the STAX-SA type was defined according to the current AL service level categorization. EJ and TK chose two domains from STAX-SA as the most important characteristics: 1) Staffing location and 2) Physical structure. These were chosen because they are also defined by law so it was possible to adjust the answers accordingly.

For example, if an AL service level was estimated to be between STAX-SA Types 2 and 3, and the current AL service level in the current three-level system was part-time assistance, the only differentiating domain is level of support. Therefore, it was assumed that because staff is available daily during the daytime the level of support is thus high, and the physical structure is a congregate setting, this AL service level would be recategorized to STAX-SA Type 2.

Table 2. Domains and response options for The Simple Taxonomy for Supported Accommodation (STAX-SA) (11)

Domain	Guidance	Response options
Staffing location	Are support staff on-site or off-site?	1. Staff on-site 2. No staff on-site
Level of support	Level of support should reflect frequency, intensity and nature of support	1. High support 2. Moderate support 3. Low support 4. No support
Move-on	How much emphasis is placed on service users moving to another less supported unit?	1. Strong emphasis on move-on 2. Limited emphasis on move-on
Physical structure	Congregate setting = Communal facilities, with other mental health users Individual accommodation= independent community housing, not mental health specific	1. Congregate setting 2. Individual accommodation

At the third stage, to evaluate the feasibility of STAX-SA categorization, each AL unit manager was asked for their perception of how well the STAX-SA Type, defined in the second stage, captured the key characteristics of the current AL service level they provided. The AL unit managers filled a web-based questionnaire, either on their own or with author EJ's assistance. The evaluation of the feasibility of STAX-SA was performed with two questions. Firstly, the AL unit managers evaluated the usability of STAX-SA in describing their services by using a 5-point Likert scale (1='Not at all', 5='Extremely') on every AL level depending on how many AL levels each manager worked with. Secondly, one open question inquired "Do you see this classification being useful in your everyday operation?" with the aim to get the AL unit manager's perception about the usefulness of STAX-SA in their AL service (11). The answers to this open question were scored into 3 categories (positive, neutral and negative) by authors EJ and TK.

RESULTS

AL UNITS PARTICIPATING IN THE STUDY

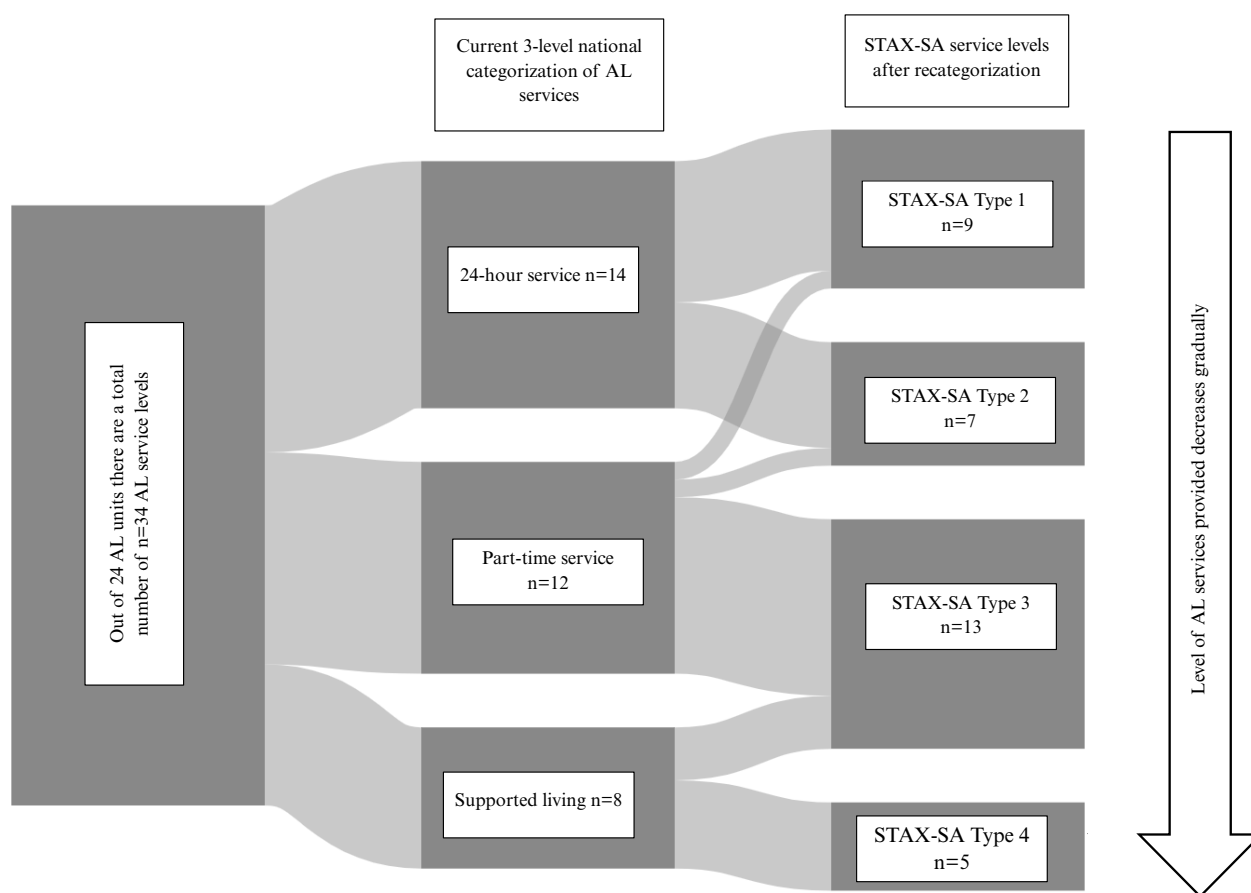
There were 25 AL units for the mentally ill in the study area, of which 23 units (92%) were willing to participate in the study. These 23 units provided a total of 34 AL services. The majority of these AL units provided AL services with 24-hour service (n=14) or part-time service (n=12), and eight units gave services for supported living (n=8).

RECATORIZATION OF AL SERVICE LEVELS ACCORDING TO STAX-SA (TYPES 1-5)

Of all 34 AL service levels provided by 23 AL units participating in this study, 64.7% (n=22) (24-hour service n=12, part-time service n=7, supported living n=3) fit perfectly to STAX-SA categorization. Further, 35.3% (n=12) of AL service levels (24-hour service n=2, part-time service n=5, supported living n=5) did not fit to STAX-SA categorization on the initial scoring.

As *Figure 2* shows, the current AL service level with 24-hour service was recategorized to STAX-SA Type 1 (57.1%) and Type 2 (42.9%). The majority of the current AL service level for part-time service was classified to be STAX-SA Type 3 (83.3%). Supported living was recategorized as Type 3 (37.5%) and Type 4 (62.5%).

Figure 2. AL service level changes after recategorization to STAX-SA. None were recategorized to STAX-SA Type 5



Note: AL: Assisted living. 24-hour service, AL level where staff is available constantly; part-time service, AL level where staff is available except during night-time; supported living, AL level where staff is available upon need. Type 1-5 are The Simple Taxonomy for Supported Accommodation (STAX-SA) categorization levels of support where Type 1 is the highest

GENDER DISTRIBUTION OF HABITANTS IN AL SERVICES

In all of the 24 AL units participating in the study there were total of 505 habitants; 58.4% were men and 41.6% women. As *Table 3a* shows, by the current AL service levels, there were 243 habitants with 24-hour service; 53.1% were men. 160 habitants were living with part-time service; 65.6% were men. There were 102 habitants in supported living; 59.8% were men.

Correspondingly, and based on the STAX-SA (*Table 3b*), STAX-SA Type 1 comprised 152 habitants; 50.7% were men. In STAX-SA Type 2, there were 95 habitants; 56.8% were men. 161 habitants were in STAX-SA Type 3; 65.2% were men. In STAX-SA Type 4 there were 97 habitants; 60.8% were men.

PSYCHIATRIC DIAGNOSES OF HABITANTS IN AL SERVICES

The distribution of diagnoses of habitants in different AL service levels and according to the STAX-SA types is presented in *Table 4*. A total of 684 diagnoses were collected among the habitants in AL services. As seen in *Table 4a*, Schizophrenia was clearly the most common diagnosis as there was a total of 230 (33.6%) schizophrenia diagnoses and 60% of these were in 24-hour services. The second most common diagnoses were affective disorders, 20.5%, which were represented somewhat evenly from 24-hour services to supported living.

After applying the STAX-SA (*Table 4b*), most of the schizophrenia diagnoses were in Type 1 (36.2%) and the least in Type 4 (12.2%). Most affective disorders were in Type 3 (37.9%) and Type 2 (25.0%).

Table 3. The gender distribution of habitants in assisted living (AL) services for the mentally ill by: a) current AL service levels, and b) according to The Simple Taxonomy for Supported Accommodation (STAX-SA) types

a) Current 3-level categorization of AL services

		Level of AL services provided decreases gradually		
Gender	N (%)	24-hour service	Part-time service	Supported living
Men	295 (58.4)	129 (53.1)	105 (65.6)	61 (59.8)
Women	210 (41.6)	114 (46.9)	55 (34.4)	41 (40.2)
Total	505 (100)	243 (100)	160 (100)	102 (100)

b) Five types of AL services according to STAX-SA

		Level of AL services provided decreases gradually				
Gender	N (%)	Type 1	Type 2	Type 3	Type 4	Type 5
Men	295 (58.4)	77 (50.7)	54 (56.9)	105 (65.2)	59 (60.8)	0 (0.0)
Women	210 (41.6)	75 (49.3)	41 (43.1)	56 (34.8)	38 (39.2)	0 (0.0)
Total	505 (100)	152 (100)	95 (100)	161 (100)	97 (100)	0 (0.0)

Table 4. The psychiatric diagnoses of habitants in assisted living (AL) services for the mentally ill by: a) current AL service levels, and b) according to The Simple Taxonomy for Supported Accommodation (STAX-SA) types

a) Current 3-level categorization of AL services

		Level of AL services provided decreases gradually		
Diagnosis	N (%)	24-hour service	Part-time service	Supported living
Schizophrenia	230 (33.6)	138 (60.0)	62 (27.0)	30 (13.0)
Other psychosis	75 (11.0)	41 (54.7)	17 (22.7)	17 (22.7)
Affective Disorders	140 (20.5)	56 (40.0)	53 (37.9)	31 (22.1)
Others	120 (17.5)	64 (53.3)	34 (28.3)	22 (18.3)
Substance Abuse	119 (17.4)	61 (51.3)	41 (34.5)	17 (14.3)
Total	684 (100)	360 (52.6)	207 (30.3)	117 (17.1)

b) Five types of AL services according to STAX-SA taxonomy

		Level of AL services provided decreases gradually				
Diagnosis	N (%)	Type 1	Type 2	Type 3	Type 4	Type 5
Schizophrenia	230 (33.6)	84 (36.5)	55 (23.9)	63 (27.4)	28 (12.2)	0 (0.0)
Other psychosis	75 (11.0)	19 (25.3)	23 (30.7)	18 (24.0)	15 (20.0)	0 (0.0)
Affective Disorders	140 (20.5)	24 (17.1)	35 (25.0)	53 (37.9)	28 (20.0)	0 (0.0)
Others	120 (17.5)	38 (31.7)	28 (23.3)	32 (26.7)	22 (18.3)	0 (0.0)
Substance Abuse	119 (17.4)	39 (32.8)	25 (21.0)	39 (32.7)	16 (13.5)	0 (0.0)
Total	684 (100)	204 (29.8)	166 (24.3)	205 (30.0)	109 (15.9)	0 (0.0)

There are more psychiatric diagnoses than habitants, because some may suffer from multiple psychiatric disorders

EVALUATION OF THE FEASIBILITY OF THE STAX-SA

17 AL unit managers participated in the STAX-SA feasibility study, representing 22 AL service levels (24-hour service n=10, part-time service n=7, supported living n=5). 86.4% scored the feasibility of STAX-SA high (scores 4-5) and the mean score of evaluations was 4.23. When calculated by different AL service levels, the mean scores were 4.70 for 24-hour service, 4.57 for part-time service and 3.00 for supported living.

15 AL unit managers also answered an open question, “Do you see this classification being useful in your everyday operation?” 14 gave a positive response for STAX-SA categorization in Type 1 and 2. All perceived that STAX-SA is useful for them to be used in practice and particularly when there is a need to describe their service to others. The AL unit managers for Type 3 and 4 service levels evaluated STAX-SA as positive and neutral. The major criticism of the AL unit managers concerned the use of STAX-SA in supported living. In their opinion some of the supported living habitants do move-on but are in need of long-term AL services.

DISCUSSION

Despite the continuous growth of assisted living (AL) in the past decades there has been little research on the effectiveness of AL in general and, in particular, on the services provided in AL (4–6,10,18,19). One of the main problems regarding AL service research has been a lack of a global unified categorization of these services, which makes comparative research difficult (5,16). Also, a comprehensive and internationally usable methodological tool for categorization has been missing. In order to uniform the methods, research is needed in which the effectiveness of international measures is tested in relation to national categorizations. In this study we were able to recategorize the current national three-level system into the new international STAX-SA five-level categorization, and examine its feasibility and usability in Finnish AL services.

Our main finding was that correspondence to STAX-SA categorization was rather good, as 64.7% of the AL service levels could be directly classified to certain STAX-SA types. Our proportion is higher compared to the recent study by Lilliehorn and workgroup 2023, in which 48% of community-based accommodation service units were completely classified to STAX-SA types (20). The strength

of STAX-SA categorization was the ability to describe the majority of the 24-hour and part-time service units. STAX-SA ability to describe AL services weakened as the level of AL service decreased, but remained reasonably in line with findings of previous studies (16,20). It is noteworthy that in our study, 86.6% of the AL unit managers perceived that STAX-SA perfectly or somewhat perfectly reflected their current AL service levels. This proportion is higher compared to 53.2% reported in the study of McPherson et al. 2018 (16). AL unit managers also suggested in open answers the usability of STAX-SA in daily operations. There are no other similar studies focusing on the feasibility of STAX-SA by using two different evaluation measures simultaneously, to the best of our knowledge.

STAX-SA categorization was able to describe the majority of the 24-hour and part-time service units. Also, the AL unit managers rated STAX-SA as very good (above 4.50) on 24-hour and part-time service. McPherson et al. 2018 findings were similar in 24-hour service (4.25), but lower in part-time service (3.9). The difference between Type 1 and 2 was solely on the domain “move-on” which indicates AL services’ emphasis on moving onwards to lighter AL services. The majority of 24-hour service (64.3%) and a small portion of part-time service (8.3%) units were Type 1 with little emphasis on move-on

STAX-SA performed weakly in identifying supported living (Likert scale 3.0), in which the habitant has to manage more independently compared to 24-hour and part-time services. In our previous research we identified the growth of supported living (21). It seems that STAX-SA lacks the features of communal services, where it is not an institutional type of living, and the level of support is low or none with little to no emphasis on move-on (16,20).

By using STAX-SA categorization to examine the distribution of diagnoses of habitants, it seems that habitants with substance abuse as well as, schizophrenia and affective disorders are more evenly distributed compared to the current three-level system. Interestingly, we found that an equal proportion of males and females were living in the most supported Type 1 units, when in all the other Types the habitants were predominantly male. This gender distribution of Type I habitants differs from those in Finnish studies on dehospitalization, showing that the majority of discharged SMI patients from long-term psychiatric hospitals were male and assumed to be in need of more support (22). Also, Räsänen et al. 2000 reported that the gender distribution of the SMI in AL did not change from discharge up to 4-year follow-up (23). This matter needs to be studied further.

The current three-level AL categorization in Finland is based on the social welfare act and aims to ensure that the severely mentally ill (SMI) receive the services they need (15). Unfortunately, it does not specify the needs of an individual suffering from mental illness or what type of service they may need in order to cope and rehabilitate from their disease, although it has been stated in national guidelines (24). STAX-SA might be a good tool to evaluate from an individual level, AL services to achieve equity for the AL service habitants.

The current national categorization has its benefits. It seems like Type 4 units, with less support, are better described in the current categorization compared to STAX-SA. Therefore, in the future there should be more research on Type 4 levels to examine what type of categorization is suitable for those units, because the growth of supported living is ongoing and there is a risk of growing custodial care in them. In this study it was not possible to examine the allocation of habitants in AL to answer whether they are in the correct AL service level or not. It is assumable that some of the habitants in Type 1, Type 2 and Type 3 could manage with less support, and there are likely also habitants in Type 4 in need of more support than they receive (7,25). It is also important to study those who have gone through AL services into independent living with no support to understand how that occurred. Nevertheless, STAX-SA comparative categorization enables a proper examination of the allocation of the SMI to AL services in a naturalistic setting to examine the effectiveness of AL services.

LIMITATIONS AND STRENGTHS

This study has several limitations. AL service unit data (Data 1) was collected from AL unit managers. The accuracy in reporting diagnoses varied from one manager to another, depending on their knowledge of mental health. This might have affected the accuracy of diagnoses. Also, the cross-sectional manner in which the data was collected raised some concerns as AL habitants' needs change over time. The feasibility of STAX-SA was based on the AL unit managers' subjective opinions. The major strength in this study is that the participation rate of AL service units was very high (96%) and also our data comprised AL units from all service providers (municipality, third-sector and private). The methodological strength is the structured questionnaires created for the purpose of gathering quantitative information on AL service units. The perception of the applicability of the STAX-SA was asked from AL unit managers by using a qualitative open-

ended question. It gave deeper insight into the benefits and disadvantages of the STAX-SA if applied in everyday work.

CONCLUSION

STAX-SA as a methodological tool has the potential to enable comparative study on AL services based on the level they provide. STAX-SA has strengths in describing AL units and the services provided in them, especially by differentiating custodial care units from rehabilitation units in AL. Despite of our finding that STAX-SA showed incompleteness in ability to describe supported living services, we considered it to be a promising structured tool for classification of AL services. This kind of tool is needed at national and international level, since it enables conduct of comparative research of AL services. In this study we were able to recategorize 64.7% of the AL service levels by using only the domain questions in STAX-SA, and the rest were able to be recategorized by investigating their current AL service level. It is notable that although STAX-SA has been available since the year 2018, it is still quite rarely used for research purposes. In conclusion, we recommend its implementation in Finland after completing a few modifications. From the STAX-SA categorization we suggest the removal of Type 5, because in Finland there are no AL units with no support, congregate setting and staff on-site. We suggest two modifications to the domains of STAX-SA: I) The response options for the level of support should range from High to No support, to suit AL services in Finland, II) the Physical setting domain should also include individual accommodation with communal setting, since that kind of accommodation is commonly used in Finland.

Supplementary Material

Supplementary data are available at [Psychiatria Fennica online](https://www.psychiatria.fennica.fi/).

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Contributions

Data extraction EJ and TK. Data visualization EJ, TK and JK. Statistical analyses HH. Methodology HH, EJ and TK. All the authors participated in the writing and editing process of the manuscript. We would like to thank Carina Siitonen and Anu Laurikkala for their efforts in collecting the contact information of AL units in Porvoo. We would like to thank Alexandra Blomqvist for helping in the Porvoo ASPA-project as well as Porvoo city communications unit for their assistance in writing and translating to Swedish the press release as well as the research information to study participants. We also thank all the AL unit managers for their efforts in Porvoo ASPA-project.

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References

1. Farkas M, Coe S. From Residential Care to Supportive Housing for People With Psychiatric Disabilities: Past, Present, and Future. *Front Psychiatry*. 2019;10.
2. Ketola J, Jahangiri E, Hakko H, Riipinen P, Räsänen S. Assisted living for mentally ill—a systematic literature review and its recommendations. *Nord J Psychiatry* [Internet]. 2021 Dec 28;1–20. Available from: <https://www.tandfonline.com/doi/full/10.1080/08039488.2021.2001568>
3. Dalton-Locke C, Marston L, McPherson P, Killaspy H. The Effectiveness of Mental Health Rehabilitation Services: A Systematic Review and Narrative Synthesis. Vol. 11, *Frontiers in Psychiatry*. Frontiers Media S.A.; 2021.
4. McPherson P, Krotofil J, Killaspy H. Mental health supported accommodation services: a systematic review of mental health and psychosocial outcomes. *BMC Psychiatry*. 2018 Dec 15;18(1):128.
5. Killaspy H, Priebe S. Research into mental health supported accommodation – desperately needed but challenging to deliver. *The British Journal of Psychiatry* [Internet]. 2021 Apr 23 [cited 2022 Jun 14];218(4):179–81. Available from: https://www.cambridge.org/core/product/identifier/S0007125020000744/type/journal_article
6. Ketola J, Jahangiri E, Hakko H, Riipinen P, Räsänen S. Assisted living for mentally ill—a systematic literature review and its recommendations. *Nord J Psychiatry*. 2021;
7. Dehn LB, Beblo T, Richter D, Wienberg G, Kremer G, Steinhart I, et al. Effectiveness of supported housing versus residential care in severe mental illness: a multicenter, quasi-experimental study. *Soc Psychiatry Psychiatr Epidemiol*. 2022;57(5).
8. Chilvers R, Macdonald G, Hayes A. Supported housing for people with severe mental disorders. *Cochrane Database of Systematic Reviews*. 2006;
9. Chilvers R, Macdonald G, Hayes A. Supported housing for people with severe mental disorders. In: Chilvers R, editor. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2002.
10. Killaspy H, White S, Dowling S, Krotofil J, McPherson P, Sandhu S, et al. Adaptation of the Quality Indicator for Rehabilitative Care (QuIRC) for use in mental health supported accommodation services (QuIRC-SA). *BMC Psychiatry*. 2016 Dec 14;16(1):101.
11. McPherson P, Krotofil J, Killaspy H. What Works? Toward a New Classification System for Mental Health Supported Accommodation Services: The Simple Taxonomy for Supported Accommodation (STAX-SA). *International Journal of Environmental Research and Public Health* 2018, Vol 15, Page 190 [Internet]. 2018 Jan 24 [cited 2022 Jan 28];15(2):190. Available from: <https://www.mdpi.com/1660-4601/15/2/190/htm>
12. Macpherson R, Shepherd G, Thyarappa P. Supported accommodation for people with severe mental illness: An update. Vol. 18, *Advances in Psychiatric Treatment*. 2012.
13. Ministry of Social Affairs and Health. Wellbeing services county [Internet]. 2021 [cited 2023 Sep 4]. Available from: <https://stm.fi/en/wellbeing-services-counties>
14. Health and social services reform [Internet]. [cited 2023 Apr 24]. Available from: <https://soteuudistus.fi/en/frontpage>
15. Social Welfare Act [Internet]. [cited 2023 Sep 4]. Available from: <https://www.finlex.fi/fi/laki/ajantasa/2014/20141301>

16. McPherson Joanna; Killaspy Helen PK. What Works? Toward a New Classification System for Mental Health Supported Accommodation Services: The Simple Taxonomy for Supported Accommodation (STAX-SA). *Int J Environ Res Public Health*. 2018;15(2):190-NA.
17. Health Care Act [Internet]. [cited 2023 Sep 4]. Available from: <https://www.finlex.fi/fi/laki/ajantasa/2010/20101326>
18. Killaspy Stefan; Bremner Stephen; McCrone Paul; Dowling Sarah; Harrison Isobel; Krotofil Joanna; McPherson Peter; Sandhu Sima; Arbuthnott Maurice; Curtis Sarah; Leavey Gerard; Shepherd Geoff; Eldridge Sandra; King Michael HP. Quality of life, autonomy, satisfaction, and costs associated with mental health supported accommodation services in England: a national survey. *Lancet Psychiatry*. 2016;3(12):1129–37.
19. Gühne U, Stein J, Weinmann S, Becker T, Riedel-Heller SG. Housing Interventions in Severe Mental Illness - International Evidence from RCTs. *Psychiatr Prax*. 2017;44(4).
20. Lilliehorn S, Fjellfeldt M, Högström E, Markström U. Contemporary Accommodation Services for People with Psychiatric Disabilities – the Simple Taxonomy for Supported Accommodation (STAX-SA) Applied and Discussed in a Swedish Context. *Scandinavian Journal of Disability Research*. 2023;25(1):92–105.
21. Jahangiri E, Kannisto G, Hakko H, Riipinen P, Räsänen Sami. Assisted living in relation to use of psychiatric inpatient and outpatient care - a 23-year time-trend analysis of national indicators from Finland. *Psychiatria fennica* . 2022;53:190–203.
22. Salokangas RKR, Saarinen S. Deinstitutionalization and Schizophrenia in Finland: I. Discharged Patients and Their Care. *Schizophr Bull*. 1998 Jan 1;24(3):457–67.
23. Räsänen S, Hakko H, Herva A, Isohanni M, Nieminen P, Moring J. Community Placement of Long-Stay Psychiatric Patients in Northern Finland. *Psychiatric Services*. 2000 Mar;51(3):383–5.
24. Suomalaisen Lääkäriseuran Duodecimin ja Suomen Psykiatriyhdistys ry:n asettama työryhmä. Schizophrenia: Current Care Guideline [Internet]. 2022 [cited 2023 Jun 8]. Available from: <https://www.kaypahoito.fi/hoi35050>
25. Mötteli S, Adamus C, Deb T, Fröbel R, Siemerikus J, Richter D, et al. Independent Supported Housing for Non-homeless People With Serious Mental Illness: A Pragmatic Randomized Controlled Trial. *Front Psychiatry*. 2022;12.



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BERGEN 4-DAY TREATMENT (B4DT) FOR OBSESSIVE-COMPULSIVE DISORDER – AN OBSERVATIONAL PILOT STUDY OF A TREATMENT PROTOCOL IN FINLAND

ABSTRACT

Background: Bergen 4-Day Treatment (B4DT) is a concentrated exposure treatment developed to treat obsessive-compulsive disorder (OCD) that has proven to be highly acceptable and effective in several countries. The objective of this pilot study was to investigate the feasibility and preliminary treatment responses of this promising treatment in a Finnish healthcare setting.

Methods: A Finnish therapist team was trained in collaboration with Norwegian B4DT therapists and developers of the method. Twenty psychiatric outpatients diagnosed with OCD and with previous OCD-specific treatment without adequate response received B4DT in HUS Helsinki University Hospital in 2022. Main outcome measure was the self-report version of Yale-Brown Obsessive-Compulsive Scale (Y-BOCS-SR) at 10 days and three months after the treatment. Before the treatment, 55% of the patients were classified as having severe to extreme OCD (Y-BOCS-SR score 26-40).

Results: At the 10-day follow-up, 56% of the treated patients reported clinically significant ($\geq 35\%$) reduction in their OCD symptoms and 28% were in remission or had only minor symptoms (Y-BOCS-SR score ≤ 13). At three-month follow-up, the numbers were 58% and 30%, respectively. Additionally, less anxiety and depressive symptoms, sleeping problems, and better psychosocial functioning and general wellbeing were reported after the treatment. Most of the patients were highly satisfied with the given treatment (Client Satisfaction Questionnaire, CSQ-8, mean score 29.2 on scale 0-32).

Conclusions: B4DT can be successfully implemented in a Finnish healthcare setting. Both patient and employee satisfaction were high. Our treatment results were somewhat more modest compared to the Norwegian studies of B4DT, in which the patient outcome has been remarkably good. However, there is a need for more detailed RCT research comparing the B4DT with other treatment options available.

KEYWORDS: B4DT, OCD, ERP, CBT, IMPLEMENTATION, INTENSIVE TREATMENT

INTRODUCTION

Obsessive-compulsive disorder (OCD) is ranked among the 10 most debilitating mental disorders by WHO, affecting 1-3% of the population, having early onset, a chronic course if untreated, and substantial psychiatric comorbidity and societal costs [1,2]. OCD manifests as obsessions, i.e., invasive unpleasant or repulsive thoughts, mental images, or urges (e.g., fear of germs or contamination, or thoughts involving taboos like sex, religion or harm), and as compulsions that are time-consuming activities performed according to a certain pattern or rule (e.g., excessive cleaning or washing, checking, or neutralizing mental rituals such as counting or praying). These aim in one way or another to reduce the anxiety associated with obsessive thoughts or to prevent an act or event that is feared to be harmful. OCD dominates and significantly limits a person's everyday life. Effective treatments are not sufficiently available. Exposure and response prevention (ERP) therapy, with or without components of cognitive behavioural therapy (CBT), has been shown to be effective and is listed as first-line treatment in international treatment guidelines [3–5]. However, despite the documented efficacy of this treatment, the effect sizes dilute from large to medium and modest at follow-ups [6,7]. Therefore, the need for new treatment modalities for this patient group is urgent.

Bergen 4-Day Treatment (B4DT) is a concentrated exposure treatment (cET)[8] developed to treat OCD. B4DT brings together several components that have been shown to be effective in OCD treatment: the cognitive-behavioural model and giving psychoeducation; learning the effective exposure method; concentrated exposure treatment (cET); structured treatment process, and a combination of the advantages of group- and individual-based treatment in one. The intensive period (four days) is given in groups of 3-6 patients with a 1:1 therapist-patient ratio. Therefore, the treatment can be seen as an individual treatment in a group setting. As described by the method's developers [9], one of the main features of B4DT is to teach the patients to actively approach whatever elicits the relevant anxiety or discomfort, and to help them systematically use the anxiety and discomfort as a cue to “LEan into The anxiety” (LET technique) instead of employing obvious or subtle avoidance. For learning this, B4DT utilizes a longer version of cET, which seems to yield better effects than standard ERP [9]. During the B4DT, the therapist typically serves as a coach for learning the LET technique in the beginning, gradually

leaving more responsibility to the patient to be their own therapist.

In Norway, the treatment has appeared to be highly acceptable and effective: as many as 94% of patients responding and 77% recovering, and corresponding figures at 12-month follow-up, 83% and 68% [10]. The effect of B4DT has been shown to last on a long-term basis, with still as many as 72% classified as recovered four years after the treatment [11]. In addition to the decreased OCD symptoms, B4DT has been shown to significantly improve symptoms of depression and generalized anxiety [8,10,12]. So far, replication studies have been done with new therapists and new samples, [10,13], in new sites [9,12] and in a few countries outside Norway [14]. Overall, the effectiveness of B4DT in previous studies has been remarkably if not exceptionally high. However, one of the main limitations of the previous research is that most of the studies have been done by the Norwegian research group who developed the method, and so far there has been only one randomized controlled trial (RCT) study on the effectiveness of B4DT in comparison to other OCD treatments, comparing B4DT with self-help or waiting list [15,16].

Availability of effective treatments for OCD is very limited in Finland and typical psychosocial treatment is weekly individual or group CBT. In both, the total amount of guided ERP during the session tends to be modest. The aim of this pilot study was to investigate the feasibility, implementation and outcome of B4DT in Finnish setting.

METHOD

SETTING

The present pilot study was done in HUS Helsinki University Hospital. The study was approved by the ethics committee of HUS (HUS/1085/2022). The treatment was delivered from June to November in 2022 as a part of standard care at HUS Psychiatry and was free of costs for the patients.

PARTICIPANTS AND THE INTERVENTION

To participate in these B4DT pilot groups, a doctor's referral and treatment contact in HUS psychiatry was required. The inclusion criteria for the treatment were: confirmed ICD-10 clinical diagnosis of OCD (F42); minimum age of 18; refractoriness to at least one adequate OCD-specific treatment (e.g., drug trial, internet-delivered CBT, individual- or group-based CBT), and motivation to do

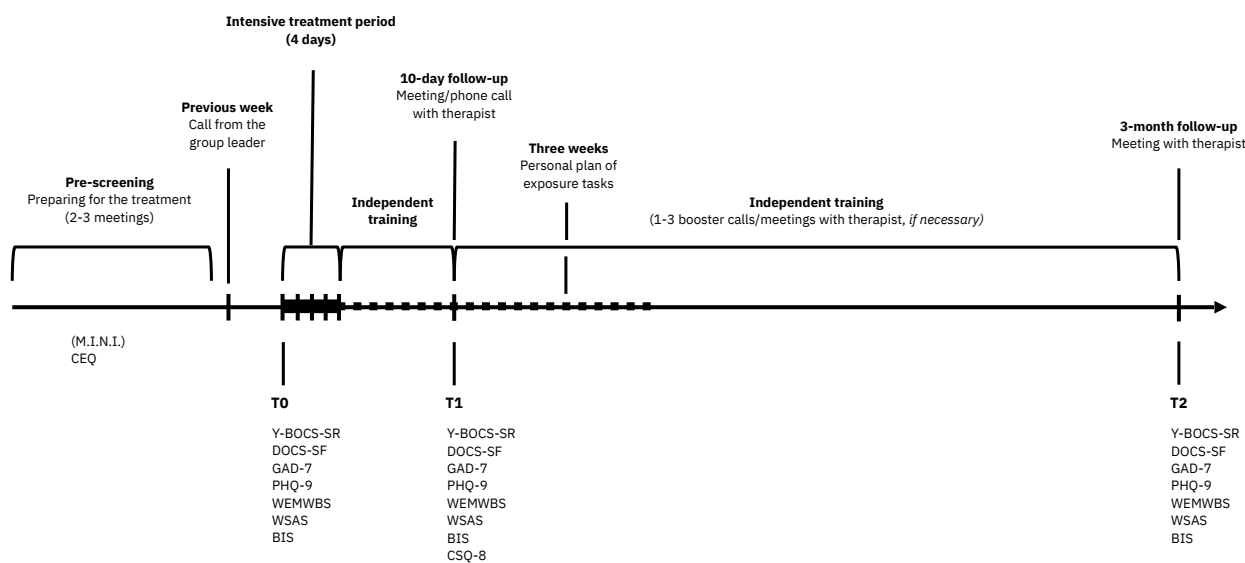
ERP. Patients gave written informed consent. Participation or non-participation had no impact on other treatment modalities or possibilities for the patients.

Only patients diagnosed with OCD according to ICD-10 criteria [17] were included in the study. The diagnosis was confirmed with Mini International Neuropsychiatric Interview (M.I.N.I.) [18] in case of any ambiguity during the pre-screening. The exclusion criteria for the study were: concurrent active psychotic or substance use disorder; imminent risk of suicide; new antidepressant or antipsychotic pharmacotherapy trial started within the last six weeks; use of benzodiazepines, other than occasionally for insomnia, and ongoing other evidence-based psychotherapy. If the patient was currently receiving psychotherapy or other psychosocial treatment for OCD, it was required to be discontinued for

the intensive 4-day treatment period and for at least three months after the treatment. As the first three pilot groups were monitored by Norwegian trainer-therapists to assure adherence to the treatment protocol, participants of these groups were required to have sufficient English skills. After that, the groups were held in Finnish.

The treatment process lasted approximately four months, including the pre-screening and preparing phase, the 4-day treatment week of cET, the follow-up period with two meetings with the therapist (10 days and three months after the 4-day treatment) as a standard procedure and 1-3 additional booster sessions if necessary (Figure 1). Self-rated data were routinely collected as a part of standard quality control procedure of HUS Helsinki University Hospital.

Figure 1. Process of B4DT before and after the intensive 4-day treatment period and used questionnaires or structured interviews in each phase of the process



Note. *M.I.N.I.* Mini International Neuropsychiatric Interview, in pre-screening, M.I.N.I. was done only if deemed necessary. *CEQ* Credibility/Expectancy Questionnaire. T0 = Pre-treatment time point on day one of the intensive treatment period, prior to concentrated exposure treatment (cET) given in days 2 and 3. At the end of day 4, a personal plan was made to support the exposure tasks for the first three weeks of independent training. T1 = 10-day follow-up, T2 = three-month follow-up, *Y-BOCS-SR*, the self-report version of Yale-Brown Obsessive-Compulsive Scale, *DOCS-SF*, Dimensional Obsessive-Compulsive Scale-Short Form, *GAD-7* Generalized Anxiety Disorder 7-item scale, *PHQ-9* Patient Health Questionnaire-9, *WEMWBS* Warwick-Edinburgh Mental Wellbeing Scale, *WSAS* Work and Social Adjustment Scale, *BIS* Bergen Insomnia Scale, *CSQ-8* Client Satisfaction Questionnaire-8

THERAPISTS AND THEIR TRAINING

Eight clinical psychologists and one psychiatrist working in the HUS Psychiatry formed the Finnish B4DT team and were trained for the treatment. All had previous experience of treating OCD patients with ERP and practices of CBT. First, a two-day psychoeducation seminar was held for the team about the main principles of the B4DT. As supervisors, the team had one of the developers of the treatment prof. Bjarne Hansen and psychologist Kristen Hagen from the Haukeland University Hospital, Bergen, Norway. After that, four treatment groups were held with 2-6 Norwegian experienced therapists in each group. In the first group, each patient had two therapists, a Finnish trainee and a Norwegian trainer. In treatment groups 2 and 3, therapist to patient ratio varied from 2:1 to 1:1, depending on the number of Norwegian trainers available. From the fourth group onwards, groups were held with Finnish therapists, with 1:1 therapist to patient ratio. In this group, the Finnish team had the possibility to consult two Norwegian therapists whenever needed. In B4DT, therapists work as a team and the therapist-patient pairs are continually evaluated. If needed, therapists could be changed to ensure better treatment for the patient. In our study, no therapist changes were made.

PRE-SCREENING PROCESS AND PREPARING PATIENTS FOR THE TREATMENT

Therapists met referred patients for 2-3 times to pre-screen their suitability for the treatment, to ascertain the severity of their OCD and to recognize possible other co-occurring psychiatric disorders, such as generalized anxiety disorder (GAD), panic disorder or personality disorders, that might affect or disturb focusing the treatment on OCD. Comorbidity was not an exclusion criterion for access to treatment, but if a disorder other than OCD clearly interfered with the patient's life more strongly, it was recommended to focus the treatment on this problem before or instead of B4DT. If no exclusion criteria were met, the therapist introduced the treatment by showing a video presenting the B4DT (<https://www.youtube.com/watch?v=nqx8knp3i4>) with Finnish subtitles. Patients' expectations for the treatment, based on the information given so far, was assessed by semi-structured interview with an adapted version of Credibility/Expectancy Questionnaire (CEQ)[19]. If the patient rated his/her expectancy or the credibility of the treatment protocol less than 70/100, the concerns and doubts were discussed with the patient to clarify possible misunderstandings.

After that, the second video presenting the outline and content of the treatment format (https://www.youtube.com/watch?v=1Fnxt0_ljpY&feature=youtu.be) was watched together with the patient. After the patient had been offered a place in the treatment group, and he/she accepted the offer, more detailed information about the treatment was given. As a preparation for the treatment, the patient was advised to make a list of relevant exposure tasks. The instruction was to find tasks that “their OCD would appreciate the least”, which often are the most relevant ones. Tasks were also briefly discussed in a phone call with the group leader a week prior to the treatment.

INTENSIVE TREATMENT PERIOD (4 DAYS)

The patients received cET, conducted over four consecutive days, in HUS Psychiatry outpatient clinic. The structure of the given treatment followed the Norwegian B4DT manual demonstrated by the Norwegian therapists. On the first day, patients participated in a 3-hour manualized psychoeducation in-group, shared their plan for individual exposure tasks and filled out the questionnaires (time point T0). In the afternoon, a voluntary one-hour psychoeducational lecture was held for the patients' family members and close ones to increase their understanding of OCD and how they can best support the patient.

Days 2-3, the focus was on individually designed, therapist-assisted exposures in as many OCD relevant settings as possible for each patient (e.g., in the polyclinic or surrounding area, in the nearby mall or at their homes). Each exposure session lasted 1-3 hours. The progress and challenges with exposure training were reported and discussed in the group meetings held in the morning, at lunch and in the afternoon. At the end of days 2 and 3, patients were advised to continue the exposures on their own. In B4DT protocol, sometimes therapist contact is offered to the patients during the evening hours, latest at 9pm. However, in our study, therapists were instructed not to contact patients in order to encourage their own independent work with OCD.

On the last day, a 3–4-hour group session was held to cover core features of the treatment and to go through the strategies to prevent and handle setbacks. Patients also had one last session with their therapist, to strengthen more independent exposure training and to make a personal plan on how to continue the exposure tasks for the next three weeks. The patients were informed on how to contact the healthcare provider if an emergency should occur during that time.

FOLLOW-UP PERIOD

All patients were offered two individual follow-up sessions with their therapist at 10 days (T1) and three months (T2) after the treatment. Therapists were instructed to schedule the follow-up times with the patient as precisely as possible for 10 days and three months after the treatment. However, especially in the three-month follow-up, there may have been a few days of variation in the implementation time due to reasons related to the patient or the therapist (e.g., illnesses, scheduling reasons). In the first follow-up the therapist met with the patient for 15-45 minutes, either by phone or in face-to-face/video meeting, and in the second follow-up for approximately 45 minutes (face-to-face/video meeting), to discuss their experiences of independent ERP training after the treatment. No exposure work was conducted in these sessions. If the patient reported any difficulties, the principles of the LET technique were repeated with an emphasis on how to find the best way for the patient to practise the method on their own. The patients were encouraged to become their own therapist, but if it was deemed necessary by the therapist and/or the therapist team at the end of the 4-day treatment or at the 10-day follow-up, 1-3 booster sessions with the therapist were offered between T1 and T2 to support their independent training. The booster sessions varied from short phone calls to 45-minute meetings that were held either by phone or face-to-face. At both follow-ups (T1 and T2) patients filled in questionnaires.

QUESTIONNAIRES

Background information. The diagnoses and medications were acquired from the electronic health record (EHR). Other background information was gathered via a questionnaire at T0 and T2 (Table 1). From the second pilot group onwards, the patients were also asked to give open written feedback about the B4DT at T2.

OCD symptoms. The primary outcome was within-individual decline in Y-BOCS-SR score before the intervention (T0) vs. after the treatment at 10 days (T1) and at three months (T2). The time points may offer slightly different kinds of information: at time point T1, severity of the reported OCD symptoms may be more related to how well the patient was able to internalize the main principles of the 4-day treatment week and managed to implement the learned skills (LET technique) to everyday life according to the plan made at the end of treatment week. If necessary, the therapist supported this process in the first follow-up

meeting and in the possible booster sessions. In contrast, reported OCD symptoms at T2 may associate more with the patient's ability to maintain the change and learned skills more independently. Y-BOCS-SR is a self-rated version of Y-BOCS consisting of 10 items that rate the severity of the patient's most prominent obsessions (items 1-5) and compulsions (items 6-10) with following parameters: time, interference, distress, resistance and control. Other used questionnaire for OCD symptoms was The Dimensional Obsessive-Compulsive Scale-Short Form (DOCS-SF), a brief (5-item) self-report measure which is less widely used but has shown to have good psychometric properties with a cut-off point of 16 identifying OCD patients from non-patients [20].

Secondary outcome measures. Anxiety symptoms were measured with the Generalized Anxiety Disorder 7-item (GAD-7) scale [21]; depressive symptoms with the Patient Health Questionnaire-9 (PHQ-9)[22]; psychosocial functioning and disability using the Work and Social Adjustment Scale (WSAS)[23]; general wellbeing with the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) [24]; sleep problems using the Bergen Insomnia Scale (BIS) [25], and patient satisfaction using the Client Satisfaction Questionnaire-8 (CSQ-8)[26].

From all the questionnaires used, three did not have a Finnish translation prior to this pilot study. Thus, DOCS-SF was translated from Norwegian, and BIS and WSAS from English into Finnish. The quality of the translation was confirmed by professional back translation.

Table 1. Descriptives of the sample (N = 20)

	n (%) / M (SD)	Range
Age	31.5 (10.5)	18–51
Women	13 (65 %)	
Single	10 (53 %)	
Education		
primary school	2 (10 %)	
vocational/high school	8 (40 %)	
lower university degree	4 (20 %)	
Master's degree	6 (30 %)	
Working/studying	13 (45 %)	
On social benefits	13 (45 %)	
Years with OCD symptoms	17.5 (8.4)	7–33
Years with OCD diagnosis	7.9 (7.4)	0–30
OCD in the family	12 (60 %)	
Previous psychotherapy	15 (88 %)	
Years of psychotherapy	5.0 (6.7)	1–24
Previous ERP	11 (65 %)	
Psychotropic medication		
antidepressants	12 (60 %)	
anti-epileptic medication	1 (5 %)	
antipsychotics	6 (30 %)	
anxiolytics	4 (20 %)	
other	8 (40 %)	



	n (%) / M (SD)	Range
Comorbidity	17 (85 %)	
GAD	4 (20 %)	
Other anxiety disorder	2 (10 %)	
Adjustment disorder	1 (5 %)	
Depression	11 (55 %)	
Personality disorder	4 (20 %)	
ADHD	2 (10 %)	
Mixed specific developmental disorder	1 (5 %)	
Obesity	2 (10 %)	
Epilepsy	1 (5 %)	
Other somatic problems	8 (40 %)	

Note: *OCD* obsessive compulsive disorder, *ERP* exposure and response prevention therapy, *GAD* generalized anxiety disorder, *ADHD* attention deficit hyperactivity disorder

STATISTICAL ANALYSES

Statistical analyses were performed with the SPSS version 25.0. [27], using repeated measures ANOVA for Y-BOCS-SR, DOCS-SF, GAD-7 and PHQ-9 with Greenhouse-Geisser corrections. Based on the previous studies of the treatment, our hypothesis was that B4DT would decrease patients' OCD symptoms. Thus, the contrasts in the analyses were pre-planned as comparisons between T0 vs. T1 and T0 vs. T2. For additional analyses comparing the patients who benefitted best from the B4DT and those whose symptoms had the least change, independent Student's t-test was conducted for the continuous variables and χ^2 test for categorical variables. Effect sizes were calculated with Cohen's d (MeanT0 – MeanT1 or T2)/SDT0[28].

With some patients, outcome variables had <10% of items missing which was deemed to be at random; in these cases, imputation was done by using mean calculated from non-missing items within the variable and within the patient. Despite the multiple reminders from the therapist, two patients did not return any of the follow-up questionnaires at T1, and one of these did not return questionnaires at T2 either. For these two patients who had all questionnaires missing at time point T1 and/or T2, imputation was not performed, so that the conclusions based on the data would not be biased in any other direction than was truly observed. Thus, these two patients were excluded from the repeated measures ANOVA.

Based on international consensus criteria [29,30], $\geq 35\%$ reduction of an individual patient's pre-treatment Y-BOCS-SR score is classified as a *clinically significant response* to the treatment. The same criterion was used for DOCS-SF. The following benchmarks are used for classifying the severity of OCD symptoms: Y-BOCS-SR score ≤ 13 points is classified as *mild symptoms/remitted*; points 14 to 25 as *moderate symptoms*, and 26-40 points as having *severe to extreme symptoms* [31]. With GAD-7 and PHQ-9, the change was classified as clinically relevant if it was at least 6 and 5 points, respectively.

RESULTS

PATIENTS

In total, 46 patients were referred to the treatment from March to November in 2022. From these, seven referrals were disqualified: due to patient's transfer outside the healthcare area covered by HUS Helsinki University Hospital; as the patient could not be reached; due to the patient cancelling the interview; due to other patient-related reasons (e.g., substance abuse, trichotillomania) or due to otherwise not fulfilling the admission criteria for the treatment, and 39 patients were taken into the pre-screening process. Of these, eight patients were excluded: due to lack of treatment motivation; for not fulfilling the diagnostic

criteria for OCD; due to use of benzodiazepines; due to language-related reasons or due to other patient-related reasons (e.g., dermatillomania, panic disorder or other symptomatology that was evaluated as a priority in the treatment). With five patients, the pre-screening process was prolonged due to their unclear treatment motivation or suitability for the treatment. The treatment was offered to the remaining 26 patients, from which 21 patients were able to attend the treatment groups covered by this pilot study. From these, one patient wished to withdraw from the study during the follow-up period and any observations received from this person were not included in the data. The descriptive statistics of the remaining 20 patients are presented in *Table 1*. The patients (65% female) were between 18 and 51 years old (Mean=31.5, SD=10.5). 70% of the patients were on psychotropic medication. 85% had other psychiatric diagnoses in addition to OCD, and 70% had more than one. The most common comorbid disorder was depression (55%). The pre-treatment Y-BOCS-SR score did not differ between the patients with or without psychotropic medication ($t(15)=.27, p=.79$), or between the patients with or without comorbid disorders ($t(18)=.36, p=.73$). On average, the patients had OCD symptoms for 17.5 years (SD=8.4) and OCD diagnose for 7.9 years (SD=7.4). Most of the patients (88%) had previously had psychotherapy, on average for 5 years (SD=6.7), and 65% had previous experience of ERP treatment.

Seven patients (35%) had at least one additional booster session with their therapist during the three-month follow-up period. Three patients received other treatment modalities from the psychiatric clinic during the follow-up: two had a previously intended 2–4-week period in the psychiatric day/outpatient ward due to psychiatric comorbidities rather than OCD alone. One patient had a short inpatient treatment due to a suicide attempt. To assess the possible association of this adverse event with the B4DT, an independent psychiatrist interviewed the patient and reviewed the patient's medical records.

OCD SYMPTOMS

Mean pre-treatment Y-BOCS-SR score was 27.90 (SD=5.67), with nine patients (45%) classified with moderate OCD and 11 patients (55%) with severe to extreme OCD. Repeated measures ANOVA found a significant effect for time after B4DT ($F(1,24)=48.14, p<.001$), and more than half of the patients had a clinically relevant decrease in their OCD symptoms ($\geq 35\%$ improvement in Y-BOCS-SR)(*Table 2*). The contrast comparisons were made against the symptoms

at pre-treatment (T0). At the 10-day follow-up (T1), 56% of the patients had responded to the treatment and 28% had reached mild symptoms/remission ($F(1,17)=64.05, p<.001, d=1.91$). After three months (T2), OCD symptoms stayed lower compared to the situation prior to the treatment ($F(1,17)=48.84, p<.001, d=1.93$): 58% had a clinically relevant response to the treatment and 30% had mild symptoms/were remitted. Post hoc comparison with Bonferroni correction was also made between T1 and T2; there were no significant changes in Y-BOCS-SR from 10-day to three-month follow-up assessment ($p=.80$). With one patient, OCD symptoms stayed severe to extreme despite the treatment at both follow-ups, and one patient was classified as remitted at 10-day follow-up but the symptoms increased to moderate at three-month follow-up (*Table 3*). In both cases, the intensity of the symptoms did not exceed the pre-treatment level. Regarding the suicidal patient, this serious adverse event was deemed unrelated to the intervention by the independent clinical reviewer.

Pre-treatment DOCS-SF scores (Mean=30.30, SD=5.55) were in line with Y-BOCS-SR, and the correlation between these two questionnaires was strong ($r=.68, p=.001$). The effect for time was also found significant for DOCS-SF ($F(2,33)=26.54, p<.001$). In test of within-subjects' post hoc contrasts, the difference between 10-day and three-month follow-up was non-significant ($p=.32$). However, the number of patients who had a clinically relevant response to the treatment measured with DOCS-SF varied between follow-ups; as many as 67% of the patients responded to the treatment in the 10 days after B4DT, but the number decreased to 32% after three months (*Table 2*).

To better understand differences between those who benefitted best from the B4DT and those whose symptoms had the least change, we further compared patients with the greatest relative improvement in OCD symptoms, as measured by the Y-BOCS-SR (at least 50% change from pre-treatment to three-month follow-up, $n=5$, range 52-72%), to patients with the smallest improvement (less than 25% change, $n=5$, range 4-24%). Due to the small number of patients in these groups, the statistical power of these comparisons is weak and can only be considered indicative. The only notable difference between these groups was in psychosocial functionality as measured with Work and Social Adjustment Scale (WSAS). Patients whose functional capacity was significantly reduced due to OCD before treatment had a weaker response than patients whose functional capacity was less affected by OCD ($t(8)=3.26, p=.012$)(*Table 4*).

SECONDARY OUTCOME MEASURES

With other symptoms, B4DT had medium to large effect based on Cohen's *d* (Table 2). In repeated measures ANOVA, within-subject effect was significant both for anxiety ($F_{2,27}=6.49, p=.008$) and depression ($F_{2,30}=9.59, p=.001$). Overall, 33% of the patients reached clinically significant change in anxiety ($GAD-7 \geq 6p$) and 44% in depressive ($PHQ-9 \geq 5p$) symptoms at 10-day follow up. At 3 months, the numbers were 42% and 32%, respectively. One patient reported clinically significant worsening (14 points change, from mild to severe) in anxiety symptoms from pre-treatment to three-month follow-up. None of the patients reported clinically significant worsening in depressive symptoms. Patients' psychosocial functioning problems and disabilities (WSAS) and sleeping difficulties (BIS) tended to decrease, and their general wellbeing (WEMWBS) to increase after B4DT. With all these three, the effect as measured by Cohen's *d* was stronger at 10-day follow-up than after three months. In general, patients were really satisfied with the given treatment (CSQ-8; Mean=29.17, SD=3.47, range 0-32), and in most cases, even if their symptoms had only minor improvement or had got worse. For example, the patient whose anxiety symptoms got significantly worse nevertheless gave full score on CSQ-8.

PATIENT FEEDBACK AND EXPERIENCES OF B4DT

A total of eight patients gave written open feedback at three-month follow-up. Most of them were grateful for getting into the treatment and said that they got at least some useful tools towards lives that are no longer ruled by OCD. Notes, handouts and different metaphors used for OCD helped some patients in maintaining the positive change during the independent learning phase, even when they had other difficulties in their lives or challenges with their mood. Two patients described how they felt confused or anxious about the free time they got back from OCD, and one mentioned being even angry and sad about the time lost because of the OCD before getting into the treatment.

As noted in our additional analyses, lower psychosocial functionality prior to the treatment might have been one factor that made it more difficult for a patient to benefit from the treatment. To learn more about the possible factors affecting the patients' treatability, six patients whose change in OCD symptoms were the smallest after receiving B4DT were offered a voluntary 30-45-minute feedback

interview in March 2023. None of these patients declined this opportunity. In these discussions, some patients wished for better pre-treatment preparation and/or for more support from their therapist. Some reported that it was difficult to focus or fully understand the given psychoeducation in the English-speaking groups. Some patients told they realized that despite the pre-treatment preparation and help from the therapists during the 4-day treatment week, they were still unwilling to let go of all their OCD rituals.

Table 2. Means and standard deviations at each time point and change in relation to the pre-treatment situation

Variable	Range	Pre-treatment (T0), n = 20		10-day follow-up (T1), n = 18				3-month follow-up (T2), n = 19			
		Mean	SD	Mean	SD	<i>d</i>	% CRC Δ	Mean	SD	<i>d</i>	% CRC Δ
OCD symptoms											
Y-BOCS-SR	0–40	27,9	5,7	17,1	5,9	1,91	56 %	17,0	5,8	1,93	58 %
DOCS-SF	0–40	30,3	5,5	17,9	7,6	2,23	67 %	20,0	9,5	1,86	32 %
Secondary outcomes											
GAD-7	0–21	15,4	4,6	11,0	6,0	0,96	33 %	10,8	6,4	1,01	42 %
PHQ-9	0–27	14,6	6,2	10,2	6,6	0,71	44 %	10,4	6,7	0,67	32 %
WEMWBS	4–70	37,9	8,9	45,1	9,0	0,81	-	42,4	8,5	0,52	-
WSAS	0–40	25,1	8,1	17,4	10,5	0,94	-	18,7	11,3	0,78	-
BIS	0–42	20,4	9,4	14,7	8,6	0,61	-	15,7	10,5	0,50	-
CSQ-8	0–32			29,2	3,5						

Note. *GAD-7* Generalized Anxiety Disorder 7-item scale, *PHQ-9* Patient Health Questionnaire-9, *WSAS* Work and Social Adjustment Scale, *WEMWBS* Warwick-Edinburgh Mental Wellbeing Scale, *BIS* Bergen Insomnia Scale, *CSQ-8* Client Satisfaction Questionnaire-8, *d* = Effect sizes calculated with Cohen's d $[(\text{MeanT0} - \text{MeanT1 or T2})/(\text{SDT0})]$, % CRC Δ = Percentage of cases with clinically reliable change from T0. For Y-BOCS-SR and DOCS-SF, this accounts for $\geq 35\%$ change; for GAD-7, $\geq 6p$ change; and for PHQ-9 $\geq 5p$ change

Table 3. Comparison of clinical improvement rates in Y-BOCS-SR at pre-treatment (T0), 10-day follow-up (T1) and three-month follow-up (T2). Number of patients (%)

Variable	Pre-treatment			Total
	Mild symptoms/remitted	Moderate	Severe to extreme	
	0 (0 %)	9 (45 %)	11 (55 %)	20 (100 %)
10-day follow-up				
Mild symptoms/remitted	0 (0 %)	3 (17 %)	2 (11 %)	5 (28 %)
Moderate	0 (0 %)	6 (33 %)	5 (28 %)	11 (61 %)
Severe to extreme	0 (0 %)	0 (0 %)	2 (11 %)	2 (11 %)
Total	0 (0 %)	9 (50 %)	9 (50 %)	18 (100 %)
3-month follow-up				
Mild symptoms/remitted	0 (0 %)	4 (21 %)	2 (11 %)	6 (32 %)
Moderate	0 (0 %)	5 (26 %)	7 (37 %)	12 (63 %)
Severe to extreme	0 (0 %)	0 (0 %)	1 (5 %)	1 (5 %)
Total	0 (0 %)	9 (47 %)	10 (53 %)	19 (100 %)

Note. Y-BOCS-SR: mild symptoms/remitted = ≤13p, moderate = 14-25p, severe to extreme = 26-40p

Table 4. Comparison of patients whose relative change in Y-BOCS-SR from pre-treatment (T0) to three-month follow-up (T2) was the greatest (>50%) and the smallest (<25%)

Variable	> 50% (n=5)	< 25 % (n=5)	Test statistic	P value
	n (%) / M (SD)	n (%) / M (SD)		
Age	32.4 (8.2)	32.0 (6.3)	t8 = -0.860	.93
Women	4 (80%)	3 (60%)	$\chi^2_1 = 0.476$.49
Years with OCD symptoms	20.8 (9.3)	18.0 (3.9)	t6 = -0.544	.61
Years with OCD diagnosis	9.2 (5.2)	5.8 (7.5)	t8 = -0.832	.43
OCD in the family	3 (60%)	2 (40%)	$\chi^2_1 = 0.400$.53
Years of psychotherapy	10.0 (8.9)	3.3 (2.1)	t5 = -1.512	.19
Previous ERP	2 (50%)	3 (60%)	$\chi^2_1 = 0.090$.76
Psychotropic medication	3 (75%)	2 (50%)	$\chi^2_1 = 0.533$.47
Comorbidity	5 (100%)	4 (80%)	$\chi^2_1 = 1.111$.29
Other symptoms prior to the treatment				
GAD-7	15.6 (5.0)	16.2 (5.6)	t8 = 0.178	.86
PHQ-9	11.2 (8.3)	17.8 (4.9)	t8 = 1.523	.17
WEMWBS	38.2 (9.8)	34.0 (8.5)	t8 = -0.724	.49
WSAS	18.4 (8.2)	31.8 (4.1)	t8 = 3.260	.012
BIS	20.8 (13.4)	23.2 (7.3)	t8 = 0.352	.73
Booster meetings/extra care during the follow-up	1 (20%)	3 (60%)	$\chi^2_1 = 1.667$.20

Note. *ERP* Exposure and response prevention therapy, *GAD-7* Generalized Anxiety Disorder 7-item scale, *PHQ-9* Patient Health Questionnaire-9, *WSAS* Work and Social Adjustment Scale, *WEMWBS* Warwick-Edinburgh Mental Wellbeing Scale, *BIS* Bergen Insomnia Scale, *CSQ-8* Client Satisfaction Questionnaire-8

DISCUSSION

The aim of this pilot study was to test the feasibility of B4DT in a Finnish psychiatric care environment. Based on our results, we were able to implement the method and most of our patients reported significant decrease in their OCD symptoms after receiving B4DT. Additionally, some patients experienced decreased anxiety and depressive symptoms, and reported fewer psychosocial functioning problems, less sleeping difficulties and better general wellbeing in comparison to their situation prior to the treatment. Most of the patients were highly satisfied with the treatment. The associations we found were more modest compared to previous effectiveness and implementation studies of B4DT [8,10,14]. However, considering OCD's status as a significantly debilitating and chronic mental disorder [1], the effect sizes we observed for B4DT in this pilot study were promisingly stronger or at least comparable with effect sizes found for other treatment formats that are currently commonly used, such as therapist-administered CBT and ERP [6,32–35] or internet-delivered therapies and other technology-assisted (self-guided or assisted) therapies [32,36–38].

In most psychiatric disorders, the more chronic and treatment resistant the disorder is, the weaker prognosis for the treatability tends to be. Regarding OCD, higher level of comorbid anxiety, higher OCD severity, unemployment and being single have previously been shown to associate with worse outcome of CBT [39]. According to the developers of B4DT, duration, type or difficulty of OCD symptoms or comorbidity should not significantly weaken the possibility to benefit from the treatment if the patient's motivation and readiness for change are otherwise sufficient. Still, higher depressive symptoms and longer duration of OCD symptoms prior to the B4DT can have an impact on the odds for a long-term recovery [11]. Furthermore, the impact of B4DT has been notably high even when the therapists have been new to the treatment [9,12,14]. None of our patients reported worsened OCD symptoms after the treatment, but in comparison to those who benefitted comprehensively from the B4DT, some patients had only modest change. Regarding secondary outcomes, only one of the patients reported clinically significant worsening in anxiety symptoms, and none of the patients reported clinically significant worsening in depressive symptoms. During the follow-up, three of the patients had extra treatment, none of which seemed to be related to the B4DT, but more to the patients' other psychiatric comorbidities. However, we cannot completely

exclude the possibility of adverse effects associated with the treatment.

TO WHOM AND WHEN – POSSIBLE RISK FACTORS AFFECTING THE TREATMENT OUTCOME

Several issues were raised, both in the experiences we received from the patients and in discussions with Finnish and Norwegian therapists, when reflecting the implementation process and effectiveness of B4DT. One risk factor for not benefitting from the treatment as expected might be the high impact of OCD on patients' psychosocial functioning prior to the treatment, as indicated in our supplementary analyses. Another relevant risk factor based on our experiences was lack of motivation or readiness for change. With some patients, the motivation and readiness to let go of all their OCD symptoms may easily be positively misjudged in the pre-screening process. Since many patients had numerous insufficient treatment attempts in their anamnesis, B4DT appears often as the last resort. This might feed unrealistic hopes for the effectiveness of the treatment, even without the patient's own investment, and may thus expose to disappointment if high expectations are not completely fulfilled. For some, the rapid disappearance of OCD symptoms that had dominated their lives for years, if not decades, could have been difficult to adapt to and may have brought up a wide range of mixed feelings, varying from gratitude and relief to anger and sadness, as mentioned in the open feedback we received. And for some, the transition from intensive 4-day exposure to independent training might have been too challenging due to their overall condition and level of functionality, despite the possible booster sessions. Considering the relatively large resources required by the treatment, it is essential to carefully examine for whom and in which situation B4DT should be targeted. The pre-screening skills should be thoroughly covered in the training of a new treatment team.

LEARNING AND IMPLEMENTING B4DT – THE THERAPISTS' PERSPECTIVE

The consensus in the Finnish therapist team was that the concept and main principles of B4DT may not be complicated, but implementing this new treatment into practice required tolerance for uncertainty, commitment to the training and treatment process and flexibility with the normal work routines. The pre-screening phase and building patients' trust for the treatment takes multiple meetings.

Based on the feedback from the therapist team, patients and Norwegian colleagues, sufficient time should be used for this phase of the treatment and training in it. Especially with patients whose lives have been significantly narrowed by OCD or other possible comorbid reasons, it may be necessary to think definitively about what could bring content and joy to their lives after the OCD symptoms have disappeared. This supports not only treatment motivation and maintenance of change, but also orientates patients towards a post-treatment OCD-free life. The patients' expectations for the treatment should be encouraged to be optimistic and goal orientated, yet realistic – the key for change is given during the 4-day intensive training week, but what is decisive is which choices the patient is ready to make and which changes to maintain. The final decision to participate in the treatment should always come from the patient, but if the regular B4DT format does not seem appropriate despite all the preparation, other treatment possibilities should be considered (e.g., individual B4DT intervention, or other forms of OCD treatment). Whenever in doubt, the suitability for treatment and alternative treatment options should be discussed in therapist team meetings.

Regarding the treatment weeks, we noticed that 4-day exposure is intensive not only for the patients but also for the therapists. In comparison to typical working routines in the polyclinics, with at least short breaks between meeting the patients, the therapist teams noted that during the 4-day treatment week non-stop concentration on the patients and their treatment was required, including the lunch time and meetings before and after the patients were present. In addition to the treatment weeks and direct work with the patients, the therapist team had regular meetings to review referrals, to go through pre-screened patients and to check schedules for the upcoming treatment groups. All of this requires time, resources and flexibility both from the therapist and their employer(s). In the B4DT process, many emotions were experienced together with the patients, such as struggle and doubt but also relief and amazement from the decisions patients made during the treatment. We found the close collaboration with Norwegian experts as a huge strength during the training period. The two-day seminar at the beginning of the training process shed light on the concept of the treatment. However, most of the learning took place when working with the patients and throughout the implementation process. The therapist team found that learning the LET technique and treatment protocol of B4DT were also useful for working with patients who have

other anxiety-related disorders, such as social anxiety or panic disorder.

LIMITATIONS AND OPEN QUESTIONS

One of the main limitations of this observational study is the lack of a control group, and as a consequence there is an inevitable uncertainty in the possible causal relationships between B4DT and decreased OCD symptoms. We noticed a decreasing effect in most patients' symptoms after receiving B4DT. This observed improvement might, however, also be due to several factors other than B4DT, such as high motivation for change and to be treated, or spontaneous recovery or regression towards mean. The pre-screening process followed the B4DT protocol, where patient expectancies for the treatment are evaluated with CEQ and should be at least 70/100 before taking the patient into the treatment. One purpose of this is to notice possible misunderstandings regarding the treatment so that these issues can be discussed and clarified together with the patient. However, screening and reinforcing the positive expectations for the treatment among the patients can have an impact on both therapeutic alliance and ultimately even treatment outcomes [40,41].

Secondly, the sample size of our study was smaller than we hoped for, which partly reflects the challenges during the implementation and treatment process, such as variance in the flow of referrals and time available for the pre-screening process, as Finnish therapists participated in B4DT training and treatment alongside their other outpatient work. The data from the patients who did not return the questionnaires at the given time point could have been filled by using imputation. However, the patients of our study were rather heterogeneous in terms of their age, psychiatric symptoms and other background variables. Thus, we refrained from imputation for the data of these patients in order to have an honest picture of the results and our implementation process.

Another limitation of our study concerns Y-BOCS, which was based on the self-rated version. Strong correspondence has been shown between the Y-BOCS and Y-BOCS-SR; however, the self-rated version tends to generate somewhat lower scores relative to the clinically administered Y-BOCS, especially with patients with severe depression [42]. As over half of our patients had a comorbid depression, there may have been some bias in their reported OCD symptoms. However, the other questionnaire focusing on OCD symptoms (DOCS-SF) supported the finding that we were able to focus the treatment on OCD. In the future, we aim to supplement

the assessment of the patients' OCD symptoms pre- and post-treatment with the clinically interviewed Y-BOCS. This would enable the possibility to also compare the results obtained with Y-BOCS and Y-BOCS-SR.

CONCLUSIONS

We have in this feasibility study shown that B4DT can be successfully implemented in a Finnish psychiatric healthcare setting, and that most of the patients who received the treatment reported decreased OCD symptoms. However, patients' readiness and motivation to make and maintain the change appeared to be essential in terms of the effectiveness of the treatment. In order to evaluate the clinical impact, targeting and cost efficacy of this promising treatment, more studies are needed. Implementation data from outside the HUS region would support this and contribute to the national availability of the treatment. As a pilot study and with a focus on feasibility of the treatment in Finland, we did not have a control group, and this was not a randomized treatment trial. Thus, we are not yet able to reliably evaluate the effectiveness of the treatment or causality between B4DT and decreased OCD symptoms, and for this reason, the need for randomized and controlled follow-up research is important in the future. Furthermore, it would be enlightening to compare the implementation processes and results with other clinics new to the B4DT, possibly outside the Nordic countries. As the B4DT concentrated exposure treatment has successfully been adapted to other anxiety-related disorders like panic disorder and depression [43–46], the method also offers possibilities for wider application areas within psychiatry.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

E.S., H.H. and S.S. participated in the treatment protocol as therapists. S.S. also had a role of Finnish therapist team's consultant psychiatrist. Study design and preparation for the study, including the translation process with questionnaires, was done by E.S., E.I. and S.S. The data formation and analysis were done by E.S. All the co-authors participated in the writing process by commenting the manuscript prior to submission.

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References

1. Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. *Mol Psychiatry*. 2010 Jan;15(1):53–63.
2. Hollander E, Stein DJ, Kwon JH, Rowland C, Wong CM, Broatch J, et al. Psychosocial Function and Economic Costs of Obsessive-Compulsive Disorder. *CNS Spectr*. 1997 Dec;2(10):16–25.
3. Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Van Ameringen M, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry*. 2014;14(Suppl 1):S1.
4. Koran LM. Treatment of Patients With Obsessive-Compulsive Disorder. 2010. (96).
5. NICE. Obsessive-compulsive disorder and body dysmorphic disorder: treatment. National Institute for Health and Care Excellence (NICE); 2005.
6. Olatunji BO, Davis ML, Powers MB, Smits JAJ. Cognitive-behavioral therapy for obsessive-compulsive disorder: A meta-analysis of treatment outcome and moderators. *J Psychiatr Res*. 2013 Jan;47(1):33–41.
7. Öst LG, Havnen A, Hansen B, Kvale G. Cognitive behavioral treatments of obsessive-compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. *Clin Psychol Rev*. 2015 Aug;40:156–69.
8. Havnen A, Hansen B, Öst LG, Kvale G. Concentrated ERP delivered in a group setting: An effectiveness study. *J Obsessive-Compuls Relat Disord*. 2014 Oct;3(4):319–24.

9. Kvale G, Hansen B, Björgvinsson T, Børtveit T, Hagen K, Haseth S, et al. Successfully treating 90 patients with obsessive compulsive disorder in eight days: the Bergen 4-day treatment. *BMC Psychiatry*. 2018 Dec;18(1):323.
10. Hansen B, Hagen K, Öst LG, Solem S, Kvale G. The Bergen 4-Day OCD Treatment Delivered in a Group Setting: 12-Month Follow-Up. *Front Psychol*. 2018 May 3;9:639.
11. Hansen B, Kvale G, Hagen K, Havnen A, Öst LG. The Bergen 4-day treatment for OCD: four years follow-up of concentrated ERP in a clinical mental health setting. *Cogn Behav Ther*. 2019 Mar 4;48(2):89–105.
12. Launes G, Laukvik IL, Sunde T, Klovning I, Hagen K, Solem S, et al. The Bergen 4-Day Treatment for Obsessive-Compulsive Disorder: Does It Work in a New Clinical Setting? *Front Psychol*. 2019 May 17;10:1069.
13. Havnen A, Hansen B, Öst LG, Kvale G. Concentrated ERP Delivered in a Group Setting: A Replication Study. *Behav Cogn Psychother*. 2017 Sep;45(5):530–6.
14. Davíðsdóttir SD, Sigurjónsdóttir Ó, Ludvigsdóttir SJ, Hansen B, Laukvik IL, Hagen K, et al. Implementation of the Bergen 4-Day Treatment for Obsessive Compulsive Disorder in Iceland. *Clin Neuropsychiatry*. 2019 Feb;16(1):33–8.
15. Launes G, Hagen K, Sunde T, Öst LG, Klovning I, Laukvik IL, et al. A Randomized Controlled Trial of Concentrated ERP, Self-Help and Waiting List for Obsessive-Compulsive Disorder: The Bergen 4-Day Treatment. *Front Psychol*. 2019 Nov 15;10:2500.
16. Launes G, Hagen K, Öst LG, Solem S, Hansen B, Kvale G. The Bergen 4-Day Treatment (B4DT) for Obsessive-Compulsive Disorder: Outcomes for Patients Treated After Initial Waiting List or Self-Help Intervention. *Front Psychol*. 2020 May 27;11:982.
17. World Health Organization. International statistical classification of diseases and related health problems (10th ed.) [Internet]. 2016. Available from: <https://icd.who.int/browse10/2016/en>
18. Sheehan DV, Lecubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. Development and validation of a structured diagnosis psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry C*. 1998(59):22–3.
19. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry*. 2000 Jun;31(2):73–86.
20. Eilertsen T, Hansen B, Kvale G, Abramowitz JS, Holm SEH, Solem S. The Dimensional Obsessive-Compulsive Scale: Development and Validation of a Short Form (DOCS-SF). *Front Psychol*. 2017 Sep 5;8:1503.
21. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Arch Intern Med*. 2006 May 22;166(10):1092.
22. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med*. 2001 Sep;16(9):606–13.
23. Mundt JC, Marks IM, Shear MK, Greist JM. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. *Br J Psychiatry*. 2002 May;180(5):461–4.
24. Tennant R, Hiller L, Fishwick R, Platt S, Joseph S, Weich S, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*. 2007 Dec;5(1):63.

25. Pallesen S, Bjorvatn B, Nordhus IH, Sivertsen B, Hjørnevik M, Morin CM. A New Scale for Measuring Insomnia: The Bergen Insomnia Scale. *Percept Mot Skills*. 2008 Dec;107(3):691–706.
26. Attkisson C. The Client Satisfaction Questionnaire (CSQ) Scales. In: *Measures for Clinical Practice: A Sourcebook*. 1996.
27. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Armonk, NY; 2017.
28. Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. *Psychol Methods*. 2002;7(1):105–25.
29. Farris SG, McLean CP, Van Meter PE, Simpson HB, Foa EB. Treatment Response, Symptom Remission, and Wellness in Obsessive-Compulsive Disorder. *J Clin Psychiatry*. 2013 Jul 15;74(07):685–90.
30. Mataix-Cols D, de la Cruz LF, Nordsletten AE, Lenhard F, Isomura K, Simpson HB. Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. *World Psychiatry*. 2016 Feb;15(1):80–1.
31. Storch EA, De Nadai AS, Conceição Do Rosário M, Shavitt RG, Torres AR, Ferrão YA, et al. Defining clinical severity in adults with obsessive-compulsive disorder. *Compr Psychiatry*. 2015 Nov;63:30–5.
32. Dèttore D, Pozza A, Andersson G. Efficacy of Technology-delivered Cognitive Behavioural Therapy for OCD Versus Control Conditions, and in Comparison with Therapist-Administered CBT: Meta-Analysis of Randomized Controlled Trials. *Cogn Behav Ther*. 2015 May 4;44(3):190–211.
33. Fisher PL, Cherry MG, Stuart T, Rigby JW, Temple J. People with obsessive-compulsive disorder often remain symptomatic following psychological treatment: A clinical significance analysis of manualised psychological interventions. *J Affect Disord*. 2020 Oct;275:94–108.
34. Gava I, Barbui C, Aguglia E, Carlino D, Churchill R, De Vanna M, et al. Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD). *Cochrane Common Mental Disorders Group, editor. Cochrane Database Syst Rev [Internet]*. 2007 Apr 18 [cited 2023 May 1]; Available from: <https://doi.wiley.com/10.1002/14651858.CD005333.pub2>
35. Reid JE, Laws KR, Drummond L, Vismara M, Grancini B, Mpavaenda D, et al. Cognitive behavioural therapy with exposure and response prevention in the treatment of obsessive-compulsive disorder: A systematic review and meta-analysis of randomised controlled trials. *Compr Psychiatry*. 2021 Apr;106:152223.
36. Percy CP, Anderson RA, Egan SJ, Rees CS. A systematic review and meta-analysis of self-help therapeutic interventions for obsessive-compulsive disorder: Is therapeutic contact key to overall improvement? *J Behav Ther Exp Psychiatry*. 2016 Jun;51:74–83.
37. Schröder J, Werkle N, Cludius B, Jelinek L, Moritz S, Westermann S. Unguided Internet based cognitive behavioral therapy for obsessive compulsive disorder: A randomized controlled trial. *Depress Anxiety*. 2020 Dec;37(12):1208–20.
38. Wootton BM, Karin E, Titov N, Dear BF. Self-guided internet-delivered cognitive behavior therapy (ICBT) for obsessive-compulsive symptoms: A randomized controlled trial. *J Anxiety Disord*. 2019 Aug;66:102111.
39. Knopp J, Knowles S, Bee P, Lovell K, Bower P. A systematic review of predictors and moderators of response to psychological therapies in OCD: Do we have enough empirical evidence to target treatment? *Clin Psychol Rev*. 2013 Dec;33(8):1067–81.

40. Enck P, Zipfel S. Placebo Effects in Psychotherapy: A Framework. *Front Psychiatry*. 2019 Jun 26;10:456.
41. Windle E, Tee H, Sabitova A, Jovanovic N, Priebe S, Carr C. Association of Patient Treatment Preference With Dropout and Clinical Outcomes in Adult Psychosocial Mental Health Interventions: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2020 Mar 1;77(3):294.
42. Storch EA, Nadeau JM, De Nadai AS, Cepeda SL, Riemann BC, Seibell P, et al. Symptom correspondence between clinicians and patients on the Yale–Brown Obsessive Compulsive Scale. *Compr Psychiatry*. 2017 Feb;73:105–10.
43. Iversen HM, Eide TO, Harvold M, Solem S, Kvale G, Hansen B, et al. The Bergen 4-day treatment for panic disorder: replication and implementation in a new clinic. *BMC Psychiatry*. 2022 Nov 23;22(1):728.
44. Kvale G, Wilhelmsen-Langeland A, Jürgensen M, Hystad SW, Öst LG, Søfteland E, et al. Concentrated transdiagnostic and cross-disciplinary group treatment for patients with depression and with anxiety: a pilot study. *BMC Psychiatry*. 2022 Sep 5;22(1):587.
45. Frisk B, Njøten KL, Aarli B, Hystad SW, Rykken S, Kjosås A, et al. A Novel Concentrated, Interdisciplinary Group Rehabilitation Program for Patients With Chronic Obstructive Pulmonary Disease: Protocol for a Nonrandomized Clinical Intervention Study. *JMIR Res Protoc*. 2022 Oct 26;11(10):e40700.
46. Eide TO, Hjelle KM, Sætre IU, Solem S, Olsen T, Sköld RO, et al. The Bergen 4-day treatment for panic disorder: implementation in a rural clinical setting. *BMC Psychiatry*. 2023 May 1;23(1):305.

LETTER TO THE EDITOR

TIMO PARTONEN, HASSE KARLSSON, ERKKI ISOMETSÄ

TO THE EDITOR

ABSTRACT

We present a case study of scientific publishing which we base on a line of discussion we had in the official journal of the International Behavioral Neuroscience Society having the Journal Impact Factor of 8.2 as of 2022, which places it a Q1 journal in the categories of behavioural sciences (the 5th out of 54) as well as neurosciences (the 37th out of 306). Here, we quote the incorrect or inaccurate claims, check their data and comment each one by one.

KEYWORDS: BIPOLAR DISORDER, ETHICAL GUIDELINES, PEER REVIEW, SCIENTIFIC PUBLISHING

In the official journal of the International Behavioral Neuroscience Society, a review [1] stated that bipolar disorder results from contemporary Western lifestyles causing neuroinflammation. The facts as they were provided did not support this statement. We sent a commentary [2] on the review [1], to which the authors of the review [1] responded [3] with inappropriate phrases which suggested unethical intent that went beyond polite disagreement as judged by the Editor's note [4] in the end. In addition to the inappropriate phrases, the response [3] contained incorrect or inaccurate claims which were left uncorrected in the literature. Here, we quote the claims, check their data and comment each one by one.

ONE

CLAIM: "In their commentary [<https://doi.org/10.1016/j.neubiorev.2021.09.039>], Partonen and colleagues argued that the prevalence of bipolar disorder is similar in people with contemporary western lifestyles and in people with traditional lifestyles. As the main piece of evidence, they cited Georgi et al. (2014), who argued that "bipolar type 1 and 2 disorders in the Amish occur with similar prevalence, pattern of symptoms, clinical course and response to mood-stabilizing medicines as observed in the general North American population". This is clearly incorrect, because none of the three references

cited by Georgi et al. (2014) to support this claim studied population prevalence of bipolar disorder (BD) among the Old Order Amish."

COMMENT: The claim One is incorrect. The main piece of evidence is collected from the 1970s (Egeland, 1983) to the 2010s (Georgi et al., 2014, in which Egeland is a co-author). The three references cited by Georgi et al. (2014) in PLoS Genetics are as follows.

First, Hostetter et al. of 1983 in *American Journal of Psychiatry* studied diagnostic stability to determine validity of diagnosis, reported the agreement on 120 Amish cases, and observed the course of the illness to verify subsequent episodes of bipolar type 1 disorder and bipolar type 2 disorder.

Second, Pauls et al. of 1992 in *Archives of General Psychiatry* reported [quote]: "Active cases of mental disorder were ascertained in two ways during the period 1976 through 1987: (1) a survey of all Amish patients admitted to the psychiatric inpatient facilities serving the area; and (2) a community epidemiologic survey of all families [of the old-order Amish community of Lancaster County, Pennsylvania]. A total of 206 cases of mental illness were identified through these methods ... Forty active cases were diagnosed by the psychiatric board as BP I ... eight had a diagnosis of bipolar II ... Total census data are available for the Amish; thus, it

is possible to estimate age- and sex-specific prevalences for each of these disorders. These rates will be underestimates of the true rates of illness to the extent that a lifetime diagnosis will be missed if no episodes of illness occurred during the time frame of this study ... The number of first-degree relatives receiving each of the six diagnoses is presented in *Table 2*, together with the uncorrected and age-corrected rates for each diagnosis. These rates are comparable with others reported in the literature and are significantly higher than the age-corrected prevalence estimates [of $1.2 \pm 0.1\%$ for bipolar type 1 disorder and $0.2 \pm 0.1\%$ for bipolar type 2 disorder] from this population (see *Table 1*.)”

Third, Egeland of 1994 is an overview entitled “An Epidemiologic and Genetic Study of Affective Disorders among the Old Order Amish” in *Genetic Studies in Affective Disorders* by Wiley-Interscience and reported [quote]: “results for a research investigation that now spans a 16-year period, and yet remains contemporary in its aims and focus ... By 1980, we reported on the ascertainment of 112 “actively ill” patient cases; 71% had a major affective disorder according to the RDC (Egeland & Hostetter, 1983). A 1986 report listed 62%, or 107 of 173 patients, as actively ill with major affective disorders (Egeland, 1986). The latest diagnostic breakdown for active cases through the past 15 years [1976–1990] is given in *Table 4-1*”. Of 221 individuals, 63 (28.5%) were diagnosed with bipolar type 1 disorder or bipolar type 2 disorder, and 6 (2.7%) with other bipolar (atypical/chronic) disorder.

In our commentary [2], we stated this as the best evidence currently available.

TWO

CLAIM: “We contacted Professor Francis J. McMahon who has led studies on genetics of BD among the Old Order Amish and he confirmed that there are no published or unpublished studies that would have recorded the prevalence of BD since the study done in 1976–1980 by Egeland and Hostetter (1983) which we originally cited [https://doi.org/10.1016/j.neubiorev.2020.12.031].”

COMMENT: The claim Two is inaccurate. The main field work for the Amish Study of Major Affective Disorders was done in 1976–1980, which was made possible by the more than 20 years of research activities among the Amish of the principal investigator (Egeland), and thereafter studies have been conducted. Data being derived from all this work, the prevalence has been estimated.

Already in the publication by Egeland and Hostetter (1983) in *American Journal of Psychiatry*, it reads that for a stable population of Lancaster County Amish aged 15 years or older [quote]: “the rate for major affective disorders is about 1%, which is half the usual rate of mood disorders in other [North American] populations ... rates for both mental illness in general and affective disorders specifically appear to be below average”.

Thereafter, in the publication by Egeland (1983) in *Comprehensive Psychiatry*, reporting the study of 1976–1982, it reads [quote]: “Since there are other active unipolar cases not yet interviewed but tagged for bipolarity, it is quite possible that the bipolar ascertainment for the Amish study will increase.” Further, it reads [quote]: “The Amish population is perhaps the first in this country, and of a European origin, reporting a high proportion of bipolar compared to unipolar illness.”

In the publication by Georgi et al. (2014) in *PLoS Genetics*, it reads [quote]: “Bipolar disorder type I (BPI) and bipolar disorder type II (BP2) in the Amish occur with similar prevalence, pattern of symptoms, clinical course and response to mood-stabilizing medicines as observed in the general North American population [17–19]”, where the three references cited were published between 1983 and 1994, of which that of Egeland of 1994 reported the prevalence rates of bipolar disorder among the Old Order Amish for 1976–1990.

In two publications where McMahon himself was the senior author, it was reported that [quote from Hou et al., 2013, in *Trends in Genetics*]: “The presentation of major psychiatric disorders among the Amish seems to be generally similar to that in other North American populations ... Large epidemiologic studies of psychiatric disorders have not, to our knowledge, been performed in this population, and therefore the true prevalence and geographic distribution of disorders are unknown”, and that [quote from Dumont et al., 2020, in *Journal of Psychiatric Research*]: “44 of the 161 participants received a BEFD of BSD (27.3%), significantly higher than the 1–2% lifetime prevalence found in the general population (Ferrari et al., 2013).” Furthermore, in the latter, the distribution of bipolar spectrum disorder cases and non-cases (both healthy and diagnosed with other psychiatric disorders) revealed that bipolar spectrum disorders were more prevalent among the Amish than Mennonite or other (or unspecified) Anabaptist groups.

THREE

CLAIM: “Partonen et al. were informed twice during the review process of their commentary that the research they cited did not study BD prevalence. However, they ignored the feedback and decided to publish their commentary anyway, repeating the error in Georgi et al. (2014).”

COMMENT: The claim Three is incorrect, because there is no error in the article by Georgi et al. (2014). Since there is not any correction nor retraction, we have no reason to question the integrity of the work by Georgi et al. (2014) as published in *PloS Genetics*. The three references cited by Georgi et al. (2014) in *PloS Genetics* included the following: Hostetter et al. of 1983 in *American Journal of Psychiatry* which reported the diagnostic agreement on 120 Amish cases and observed the course of the illness to verify subsequent episodes of bipolar type 1 disorder and bipolar type 2 disorder; Pauls et al. of 1992 in *Archives of General Psychiatry*, where the prevalence rates of bipolar type 1 disorder and bipolar type 2 disorder among the first-degree relatives of Old Order Amish bipolar type 1 disorder probands were presented and compared to the age-corrected population prevalence rates of this population; and Egeland of 1994 which provided the diagnostic breakdown for 221 active cases for 1976–1990.

FOUR

CLAIM: “Partonen et al. calculated that the difference in BD prevalence between the Amish and other US populations would have been only 4.6-fold. This is incorrect. They were comparing the 5-year prevalence in the Amish with the 1-year prevalence in other US populations. Thus, the true differences in BD prevalence between the Old Order Amish and other North American populations can be much higher, even higher than we calculated in our corrigendum (<https://doi.org/10.1016/j.neubiorev.2021.03.027>).”

COMMENT: The claim Four is incorrect. The lifetime, not the 1-year, prevalence in other US populations (2.1%) being divided by the period (5-year) prevalence in the Amish (0.46%) yielded the 4.6-fold difference that we provided in our commentary [2].

Our commentary [2] was received on 19 February 2021, received in revised form on 17 September 2021, accepted on 20 September 2021, and available online on 28 September 2021. In the version we originally submitted

as our commentary, we wrote [quote]: “The cited mental health study on the Amish included 8,186 participants, not 12,500, of whom 38, not 28, had bipolar disorder, yielding the prevalence rate of 0.46%, not 0.22%, for bipolar type 1 and 2 disorders till 1980. The cited World Mental Health Survey Initiative study revealed the lifetime prevalence rate of 2.1%, not 4.4%, for bipolar type 1 and 2 disorders in the USA in 2002–2003. So, the difference between the Amish and other US populations were 4.6-fold, not over 18-fold as stated, or in fact not more than 2-fold or less, because in the original report on the Amish the prevalence rate was estimated to be half the usual rate of mood disorders in other populations, or below average.”

The corrigendum [5] by the authors of the review [1] was received on 24 February 2021 (five days after our commentary [2] was received and sent for peer review), received in revised form on 23 March 2021, accepted on 24 March 2021, and available online on 1 April 2021. In the corrigendum [5], the authors wrote [quote]: “There was a calculation error in [<https://doi.org/10.1016/j.neubiorev.2020.12.031>]. Page 30: ‘A mental health study on 12,500 Amish people found that only 28 of them suffered from bipolar disorder (Egeland and Hostetter, 1983). This means that the likelihood of an Amish person having bipolar disorder is 0.22%. Instead, 4.4% of Americans experience this disorder (Merikangas et al., 2011). The difference between the Amish people and other Americans is therefore over 18-fold.’ The authors sincerely apologize for this error. The corrected sentences should be: ‘A mental health study on a population of 12,500 Amish people of which 8186 were adult found that only 38 suffered from type 1 or 2 bipolar disorder (Egeland and Hostetter, 1983). This means that the 5-year prevalence of the bipolar disorder is 0.46%. The WHO study found that the 1-year prevalence of bipolar disorder was 1.4% (Merikangas et al., 2011). Although it is difficult to compare the 5-year prevalence with the 1-year prevalence, one could conclude that the prevalence of the bipolar disorder is substantially lower among Older Order Amishes than in other north Americans. The true difference in prevalence is probably much larger because Egeland and Hoster (1983) noted that the “Amish interact so closely within a given district that even mild cases of emotional upset or mental disturbance cannot go undetected, and each case of mental illness was reported, on the average by 18 informants”. Thus, the WHO study and other studies have not been able to detect all possible cases of mood disorders as exhaustively as Egeland and Hoster were able to do.’ It is important to note that there is additional support for the environmental mismatch

hypothesis of bipolar disorder. For example, Nimgaonkar et al. (2000) found that only three out of 4286 participants met the diagnostic criteria of bipolar disorder in the Hutterites in 1950–1953.”

FIVE

CLAIM: “Importantly, there is much more evidence showing that BD prevalence is higher in people with contemporary western lifestyles than in people with traditional lifestyles than we presented in our original article. Unfortunately, we are not able to provide all of it here because of limitations on the length requirements and the number of citations in the response article type. To provide one notable example, a study in the Hutterites in 1950–1953 found that only three out of 4286 participants met the diagnostic criteria of bipolar disorder, as cited in our corrigendum (<https://doi.org/10.1016/j.neubiorev.2021.03.027>), which Partonen et al. ignored.”

COMMENT: The claim Five is unfair. The corrigendum [5] was submitted on 24 February 2021 and thereafter published on 1 April 2021 while the peer review of our commentary [2] was still ongoing, being started on 19 February 2021. In our commentary [2], we criticized the review [1] as it had been published, and therefore we ignored none. After the two rounds of peer review and more than seven months, our commentary [2] was published on 28 September 2021.

The subsequent claim is incorrect as well, as it was in the corrigendum [5]. In the publication by Nimgaonkar et al. (2000) in *American Journal of Psychiatry*, the prevalence rates for DSM-IV psychoses, based on a one-author review of the clinical records of 252 individuals classified as psychiatrically ill in an epidemiological survey of all Hutterites living communally in the United States and Canada on January 1, 1950, were reported, and three individuals out of 252, not out of 4286, met the criteria for bipolar type 1 disorder, not including bipolar type 2 disorder nor bipolar disorder not otherwise specified. Further, the population estimates in the province of Manitoba, Canada, for 1992–1997 yielded that the prevalence rates for ICD-9 psychoses were lower in both the Hutterites and the comparison group, but the prevalence of ICD-9 neurotic disorders was higher among both the Hutterites and the comparison group (i.e., persons with one of the 19 surnames but with non-colony residential addresses that may include Prairieleut and Hutterites who

left the colony and their descendants), as compared with the total Manitoba population.

SIX

CLAIM: “Partonen and colleagues also misled readers into thinking that there is no other evidence for the link between peripheral low-grade inflammation and neuroinflammation than what we originally provided in our review article [<https://doi.org/10.1016/j.neubiorev.2020.12.031>]”.

COMMENT: This claim Six is incorrect. In our commentary [2], we commented on what had been presented in the review [1]. We disagreed in that the causative link from low-grade inflammation to neuroinflammation was commonly known in humans, as the review [1] presented this causative link as its key and provided only one reference to its support. The reference was to an experimental model of laparotomy in mice which was to simulate the problem of some patients who suffer from cognitive dysfunction after surgery. The evidence as provided in the review [1] did not support the causative link, which we criticized in our commentary [2].

SEVEN

CLAIM: “There are many more experimental studies in non-human animals and also in humans showing the causality between peripheral low-grade inflammation and neuroinflammation (for an excellent review, see Troubat et al. (2021)). In contrast to claims by Partonen et al., there are even studies that show that peripheral injection of proinflammatory cytokines causes neuroinflammation in humans (Troubat et al., 2021).”

COMMENT: The claim Seven is incorrect.

In the review by Troubat et al. (2021) in *European Journal of Neuroscience*, there is a reference to one study (Moieni et al., 2015, in *Neuropsychopharmacology*), not studies, in which a single infusion, not injection, of low-dose endotoxin (derived from *Escherichia coli*; 0.8 ng/kg of body weight) was administered and there was no assessment of neuroinflammation.

Further, the immediate continuation of the discussion in the review by Troubat et al. (2021) including the reference to Bai et al. (2019) in *Journal of Neurology, Neurosurgery and Psychiatry*, which did not confirm the role of the

inflammatory component and thus does not support the hypothesis by the authors of the review [1], was not cited.

The discussion by Troubat et al. (2021) reads [quote]: “Interestingly, inflammation may be one of causes for the higher prevalence of depression in women, as the prevalence of autoimmune diseases (Whitacre, 2001) like depression (Grigoriadis & Robinson, 2007) is twice as high in women than in men, and these findings may reflect gender differences in basal immune activity (Chapman et al., 2009). The gender difference in terms of prevalence of MDD begins in adolescence and does not appear to be related to sex hormones (Kessler, 2003) but rather to higher sensitivity to stressful life events (Kendler, Thornton, & Prescott, 2001) or childhood psychosocial stress (Takizawa, Danese, Maughan, & Arseneault, 2015), which may be attributed to inflammation. In support of this hypothesis, women exposed to an experimental endotoxin challenge (single injection of a low dose of endotoxin from *Escherichia coli*) displayed increased levels of depressed mood and feeling of social disconnection compared to those who received placebo (Moieni et al., 2015). However, other clinical data did not confirm the potential role of this inflammatory component, as anti-inflammatory compounds (and particularly celecoxib and omega-3 fatty acids in monotherapy) were found to have no significant antidepressant effects in women, as might have been expected (Bai et al., 2019).”

EIGHT

CLAIM: “Partonen and colleagues criticized the idea that neuroinflammation plays a role in BD, failing to take note of recent advances in this area of research. A substantial amount of evidence shows that BD is associated with neuroinflammation (for a review, see Benedetti et al. (2020)). For example, in vivo positron emission tomography (PET) studies in patients with BD support the claim that these patients have neuroinflammation. Likewise, in vivo microglia characterization showed a significantly increased activation in the hippocampus of BD patients compared to healthy controls, suggesting the presence of neuroinflammation in BD patients. Furthermore, a direct association between microglia activation and neuronal damage in BD has been observed, suggesting a possible harmful effect of this neuroinflammatory condition (for a review, see Benedetti et al. (2020)).”

COMMENT: The claim Eight is inaccurate. In our commentary [2], we commented on what had been presented

in the review [1] and wrote [quote]: “The heterogeneity in published studies means that inflammation may play a role only in a small subset of patients with bipolar disorder.” The review by Benedetti et al. (2020) in *Frontiers in Psychiatry* was not included in the review [1], but it concluded that [quote]: “The objective of this review is to summarize available evidence on the connection between inflammation and BD, focusing on peripheral inflammatory markers and recent findings on their connection with other typical features of BD, to outline a general overview of the disorder. Moreover, it is meant to analyze the issues with data gathering and interpretation, given the partially contradictory and inconsistent nature of results.”

NINE

CLAIM: “It is important to note that there are more studies to support the claim that activation of the immune system (which also activates microglia cells) disrupts the functioning of the internal clock than those that we cited in our review article [https://doi.org/10.1016/j.neubiorev.2020.12.031]. For example, in the highlights of their excellent review on this topic, Hergenhan et al. (2020) wrote that “[c]ircadian clock proteins engage in direct physical interactions with inflammatory proteins. Immune factors also reciprocally exert control over circadian clock function.”

COMMENT: The claim Nine is inaccurate. In fact, there are the four highlights in the article by Hergenhan et al. (2020) in *Journal of Molecular Biology* as follows [quote]:

- “The immune system is under control of the circadian clock.
- Circadian clock proteins act as transcription factors controlling genes of the immune system.
- Circadian clock proteins engage in direct physical interactions with inflammatory proteins.
- Immune factors also reciprocally exert control over circadian clock function.”

In the article itself, it reads [quote]: “Nevertheless, all studies have shown that interruption was only temporary, for a maximum of three days, indicating that while oscillations are dampened the central clock still remains entrained to the environment during an immune response.” Further, it reads [quote]: “However, in vivo the interplay between bacterial products acting directly on the SCN and indirectly via inflammatory mediators released by the immune system is not clear.”

TEN

CLAIM: "The criticism presented by Partonen et al. about individual variation in symptom patterns of the depressive phase in BD is a classic example of a straw man argument."

COMMENT: The claim Ten is incorrect. We addressed the real subject and did not replace it with a false one.

ELEVEN

CLAIM: "This critical discussion should, however, be done to increase our collective knowledge about the topic, not to try to mislead the scientific community by presenting a flawed reading of existing evidence."

COMMENT: The claim Eleven is incorrect. We did not try to mislead the scientific community by presenting a flawed reading of existing evidence. We criticized the evidence as it was provided in the review [1].

CONCLUSION

The current evidence does not support the premises of the environmental mismatch hypothesis as it was presented in the review [1] nor in the second commentary [3] which was given in response to our commentary [2]. Furthermore, any author should refrain from being hostile or inflammatory as well as from making libelous or derogatory personal comments or unfounded accusations.

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References

Instead of citations the direct links to the publications in question are listed below.

1. <https://doi.org/10.1016/j.neubiorev.2020.12.031>
2. <https://doi.org/10.1016/j.neubiorev.2021.09.039>
3. <https://doi.org/10.1016/j.neubiorev.2022.104631>
4. <https://doi.org/10.1016/j.neubiorev.2022.104862>
5. <https://doi.org/10.1016/j.neubiorev.2021.03.027>



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